# AMERICAN JOURNAL OF OPHTHALMOLOGY

#### THIRD SERIES FOUNDED BY EDWARD JACKSON

#### CONTENTS

Heterophoria and depth perception in av	iation John V. V. Nicholls	1497
Intravenous novocain in ophthalmology Erwin E. Grossmann,	John B. Hitz, and George J. Roncke	1515
Diagnosis and treatment of glaucoma	Jonas S. Friedenwald	1523
Changes in vision during adolescence Albert	E. Sloane and J. Roswell Gallagher	1538
Effects of procaine and cocaine on iris	ld G. Scheie and Gaylord W. Ojers	1543
Ergot alkaloids and glaucoma		1551
Alloxan diabetes and the lens	ohn G. Bellows and David E. Shoch	1555
Intravenous tetraethyl ammonium chlorid	le	1564
Temporal arteritis	Gordon M. Bruce	1568
Inflammation of the orbital socket		1573
Idiopathic hyperlipemia	Edwin B. Dunphy	1579
Astigmatism test and the astigmometer .		1587
Massive intraocular hemorrhage		1591
Epidemic keratoconjunctivitis		1596
Effect of tilted lenses		1599
Fistulizing operation for glaucoma		1601
DEPAR	TMENTS	
Society Proceedings         1603           Editorials         1610           Correspondence         1614	Abstracts	1616 1620 1664

For complete table of contents see advertising page xi

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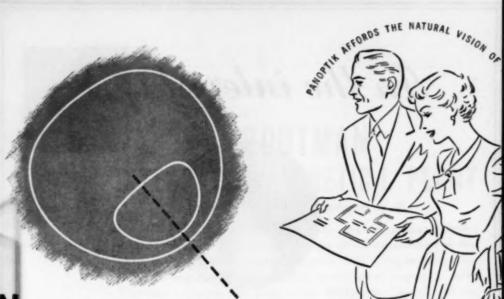
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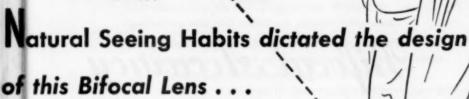
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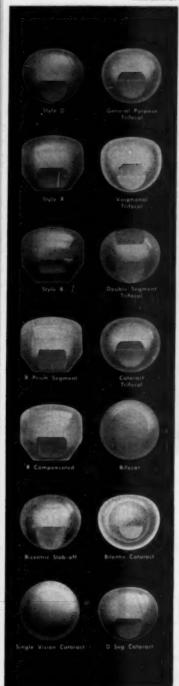
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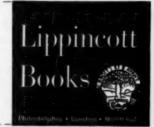
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#### CONTENTS

The use of intravenous novocain in ophthalmology. Erwin E. Grossmann, John B. Hitz, and George J. Roncke	Original Articles	
and George J. Roncke  Some problems in the diagnosis and treatment of glaucoma: The Third Mark J. Schoenberg Lecture. Jonas S. Friedenwald  Changes in vision during adolescence. Albert E. Sloane and J. Roswell Gallagher  The effects of procaine and cocaine when applied locally to the iris. Harold G. Scheie and Gaylord W. Ojers  The effects of procaine and cocaine when applied locally to the iris. Harold G. Scheie and Gaylord W. Ojers  The effect of certain hydrogenated alkaloids of ergot on glaucoma. Adolph Posner  ISA  Alloxan diabetes and the lens. John G. Bellows and David E. Shoch  Coular manifestations of intravenous tetracthyl ammonium chloride in man. Arnold P. Drucker, Max S. Sadove, and Klaus R. Unna  Temporal arteritis as a cause of blindness: Review of the literature and report of a case. Gordon M. Bruce  Gordon M. Bruce  The management of chronic inflammation of the orbital socket. John Macivor  The Crisp-Stine test for astigmatism and the Lebensohn astigmometer, George H. Stine  Massive intraocular hemorrhage following severe cerebral vascular accident. Sanders A. Goodman  NOTES, CASES, INSTRUMENTS  Epidemic keratoconjunctivitis: Report of a small office outbreak. O. J. Pellitteri and J. J. Fried  Effect of tilted lenses. Joseph I. Pascal  Epidemic keratoconjunctivitis: Report of a small office outbreak. O. J. Pellitteri and J. J. Fried  Effect of tilted lenses. Joseph I. Pascal  Epidemic keratoconjunctivitis: Report of a small office outbreak. O. J. Pellitteri and J. J. Fried  Effect of tilted lenses. Joseph I. Pascal  Epidemic keratoconjunctivitis: Report of a small office outbreak. O. J. Pellitteri and J. J. Fried  Effect of tilted lenses Joseph I. Pascal  Epidemic keratoconjunctivitis: Report of a small office outbreak. O. J. Pellitteri and J. J. Fried  Effect of tilted lenses Joseph I. Pascal  Epidemic keratoconjunctivitis  Chicago Ophthalmological Society, November 21, 1949  1600  EDITORIALS  The 16th International Congress of Ophthalmology  The Pinhole Test  Correspondence  Sudan interior mi	to the work of the Royal Canadian Air Force: Part I. John V. V. Nicholls	1497
Lecture, Jonas S. Friedenwald Changes in vision during adolescence. Albert E. Sloane and J. Roswell Gallagher The effects of procaine and cocaine when applied locally to the iris. Harold G. Scheie and Gaylord W. Ojers The effect of certain hydrogenated alkaloids of ergot on glaucoma. Adolph Posner S. Alloxan diabetes and the lens. John G. Bellows and David E. Shoch Ocular manifestations of intravenous tetraethyl ammonium chloride in man. Arnold P. Drucker, Max S. Sadove, and Klaus R. Unna Temporal arteritis as a cause of blindness: Review of the literature and report of a case. Gordon M. Bruce The management of chronic inflammation of the orbital socket. John Macivor Ocular conditions associated with idiopathic hyperlipenia. Edwin B. Dunphy The Crisp-Stine test for astigmatism and the Lebensohn astigmometer. George H. Stine Massive intraocular hemorrhage following severe cerebral vascular accident. Sanders A. Goodman  NOTES, CASES, INSTRUMENTS Epidemic keratoconjunctivitis: Report of a small office outbreak. O. J. Pellitteri and J. J. Fried Effect of tilted lenses. Joseph I. Pascal Fistulizing "Half-Elliot" operation for glaucoma. Julius Szymanski  SOCIETY PROCEEDINGS Chicago Ophthalmological Society, November 21, 1949  EDITORIALS The 16th International Congress of Ophthalmology The Pinhole Test  CORRESPONDENCE Sudan interior mission eye hospital Education of the Norwegian ophthalmologist  BOOK REVIEWS The Truth about Your Eyes Anatomy, embryology, and comparative ophthalmology; General pathology, bacteriology, immunology; Vegetative physiology, biochemistry, pharmacology, toxicology: Physiology optics, refraction, color vision; Diagnosis and therapy; Ocular motility; Conjunctiva, cornea, sclera  1620	and George J. Roncke	1515
The effects of procaine and cocaine when applied locally to the iris. Harold G. Scheie and Gaylord W. Ojers  The effect of certain hydrogenated alkaloids of ergot on glaucoma. Adolph Posner  154. The effect of certain hydrogenated alkaloids of ergot on glaucoma. Adolph Posner  155. Alloxan diabetes and the lens. John G. Bellows and David E. Shoch  Coular manifestations of intravenous tetractival ammonium chloride in man. Arnold P. Drucker, Max S. Sadowe, and Klaus R. Unna  Temporal arteritis as a cause of blindness: Review of the literature and report of a case Gordon M. Bruce  The management of chronic inflammation of the orbital socket. John Macivor  157. The management of chronic inflammation of the orbital socket. John Macivor  158. Massive intraocular hemorrhage following severe cerebral vascular accident. Sanders  A. Goodman  NOTES, CASES, INSTRUMENTS  Epidemic keratoconjunctivitis: Report of a small office outbreak. O. J. Pellitteri and J. J. Fried  159. Fried  159. Fried  159. Fried  159. Fristulizing "Half-Elliot" operation for glaucoma. Julius Szymanski  160. SOCIETY PROCEEDINGS  Chicago Ophthalmological Society, November 21, 1949  160. CORRESPONDENCE  Sudan interior mission eye hospital  Education of the Norwegian ophthalmologist  161. CORRESPONDENCE  Sudan interior mission eye hospital  Education of the Norwegian ophthalmologist  161. Color Psychology and Color Therapy  162. Anatomy, embryology, and comparative ophthalmology; General pathology, bacteriology, immunology; Vegetative physiology, biochemistry, pharmacology, toxicology; Physiology, immunology; Physiology, biochemistry, pharmacology, toxicology; Physiology optics, refraction, color vision; Diagnosis and therapy; Ocular molitity; Conjunctiva, cornea, sclera  162. Cornea, sclera  162. Cornea, sclera  163. Cornea, sclera  164. Cornea, sclera  165. Cornea, sclera  166. Cornea,	Lecture, Jonas S. Friedenwald	1523
Gaylord W. Ojers The effect of certain hydrogenated alkaloids of ergot on glaucoma. Adolph Posner The effect of certain hydrogenated alkaloids of ergot on glaucoma. Adolph Posner Aloxan diabetes and the lens. John G. Bellows and David E. Shoch Ocular manifestations of intravenous tetracthyl ammonium chloride in man. Arnold P. Drucker, Max S. Sadove, and Klaus R. Unna Temporal arteritis as a cause of blindness: Review of the literature and report of a case. Gordon M. Bruce Ison Gordon M. Bruce Gordon M. Bruce Ison The management of chronic inflammation of the orbital socket. John Macivor Ocular conditions associated with idiopathic hyperlipemia. Edwin B. Dumphy Ison The Crisp-Stine test for astigmatism and the Lebensohn astigmometer. George H. Stine Massive intraocular hemorrhage following severe cerebral vascular accident. Sanders A. Goodman Social September Septe		1538
Alloxan diabetes and the lens. John G. Bellows and David E. Shoch	Gaylord W. Ojers	1543
Ocular manifestations of intravenous tetraethyl ammonium chloride in man. Arnold P. Drucker, Max S. Sadove, and Klaus R. Unna. 1567 Temporal arteritis as a cause of blindness: Review of the literature and report of a case. Gordon M. Bruce 1567 The management of chronic inflammation of the orbital socket. John Macivor 1575 Ocular conditions associated with idiopathic hyperlipemia. Edwin B. Dunphy 1577 The Crisp-Stine test for astigmatism and the Lebensohn astigmometer. George H. Stine 1588 Massive intraocular hemorrhage following severe cerebral vascular accident. Sanders A. Goodman 1591 NOTES, CASES, INSTRUMENTS Epidemic keratoconjunctivitis: Report of a small office outbreak. O. J. Pellitteri and J. J. Fried 1592 Effect of tilted lenses. Joseph I. Pascal 1599 EDITORIALS The 16th International Congress of Ophthalmology 1602 EDITORIALS The 16th International Congress of Ophthalmology 1602 EDITORIALS The 16th International Congress of Ophthalmology 1603 Education of the Norwegian ophthalmologist 1613 Education of the Norwegian ophthalmologist 1614 Education of the Norwegian ophthalmologist 1615 Correspondence 1616 Color Psychology and Color Therapy 1618 ABSTRACTS Anatomy, embryology, and comparative ophthalmology; General pathology, bacteriology, immunology; Vegetative physiology, biochemistry, pharmacology, toxicology; Physiologic optics, refraction, color vision; Diagnosis and therapy; Ocular motility; Conjunctiva, cornea, sclera 1620		1551
Temporal arteritis as a cause of blindness: Review of the literature and report of a case. Gordon M. Bruce	Ocular manifestations of intravenous tetraethyl ammonium chloride in man. Arnold P. Drucker,	
The management of chronic inflammation of the orbital socket. John Macivor Ocular conditions associated with idiopathic hyperlipemia, Edwin B. Dumphy The Crisp-Stine test for astigmatism and the Lebensohn astigmometer. George H. Stine Massive intraocular hemorrhage following severe cerebral vascular accident. Sanders A. Goodman NOTES, CASES, INSTRUMENTS Epidemic keratoconjunctivitis: Report of a small office outbreak. O. J. Pellitteri and J. J. Fried J. Fried Seffect of titled lenses. Joseph I. Pascal Fistulizing "Half-Elliot" operation for glaucoma. Julius Szymanski SOCIETY PROCEEDINGS Chicago Ophthalmological Society, November 21, 1949 SOCIETY PROCEEDINGS The 16th International Congress of Ophthalmology The Pinhole Test CORRESPONDENCE Sudan interior mission eye hospital Education of the Norwegian ophthalmologist SOCIETY Bround International Congress of Ophthalmologist SOCIETY PROCEEDINGS The Truth about Your Eyes	Temporal arteritis as a cause of blindness: Review of the literature and report of a case.	1568
The Crisp-Stine test for astigmatism and the Lebensohn astigmometer, George H. Stine		1573
Massive intraocular hemorrhage following severe cerebral vascular accident. Sanders A. Goodman		1579
Notes, Cases, Instruments  Epidemic keratoconjunctivitis: Report of a small office outbreak. O. J. Pellitteri and J. J. Fried		1587
Epidemic keratoconjunctivitis: Report of a small office outbreak. O. J. Pellitteri and J. J. Fried		1591
J. Fried Effect of tilted lenses. Joseph I. Pascal Fistulizing "Half-Elliot" operation for glaucoma. Julius Szymanski  Society Proceedings Chicago Ophthalmological Society, November 21, 1949  Editorials The 16th International Congress of Ophthalmology The Pinhole Test  Correspondence Sudan interior mission eye hospital Education of the Norwegian ophthalmologist  Book Reviews The Truth about Your Eyes Transactions of the American Ophthalmological Society Ophthalmic Medicine Color Psychology and Color Therapy  Abstracts  Anatomy, embryology, and comparative ophthalmology; General pathology, bacteriology, immunology; Vegetative physiology, biochemistry, pharmacology, toxicology; Physiologic optics, refraction, color vision; Diagnosis and therapy; Ocular motility; Conjunctiva, cornea, sclera  1620	Notes, Cases, Instruments	
Fistulizing "Half-Elliot" operation for glaucoma. Julius Szymanski 1600  Society Proceedings Chicago Ophthalmological Society, November 21, 1949 1600  Editorials The 16th International Congress of Ophthalmology 1610 The Pinhole Test 1612  Correspondence Sudan interior mission eye hospital 1614 Education of the Norwegian ophthalmologist 1615  Book Reviews The Truth about Your Eyes 1616 Transactions of the American Ophthalmological Society 1616 Ophthalmic Medicine 1615 Color Psychology and Color Therapy 1615  Abstracts Anatomy, embryology, and comparative ophthalmology; General pathology, bacteriology, immunology; Vegetative physiology, biochemistry, pharmacology, toxicology; Physiologic optics, refraction, color vision; Diagnosis and therapy; Ocular motility; Conjunctiva, cornea, sclera 1620		1596
Chicago Ophthalmological Society, November 21, 1949		1599 1601
EDITORIALS  The 16th International Congress of Ophthalmology The Pinhole Test  CORRESPONDENCE  Sudan interior mission eye hospital Education of the Norwegian ophthalmologist  BOOK REVIEWS  The Truth about Your Eyes Transactions of the American Ophthalmological Society Ophthalmic Medicine Color Psychology and Color Therapy  ABSTRACTS  Anatomy, embryology, and comparative ophthalmology; General pathology, bacteriology, immunology; Vegetative physiology, biochemistry, pharmacology, toxicology; Physiologic optics, refraction, color vision; Diagnosis and therapy; Ocular motility; Conjunctiva, cornea, sclera	Society Proceedings	
The 16th International Congress of Ophthalmology 1612 The Pinhole Test 1612  CORRESPONDENCE Sudan interior mission eye hospital 1614 Education of the Norwegian ophthalmologist 1615  BOOK REVIEWS The Truth about Your Eyes 1616 Transactions of the American Ophthalmological Society 1616 Ophthalmic Medicine 1619 Color Psychology and Color Therapy 1619  ABSTRACTS Anatomy, embryology, and comparative ophthalmology; General pathology, bacteriology, immunology; Vegetative physiology, biochemistry, pharmacology, toxicology; Physiologic optics, refraction, color vision; Diagnosis and therapy; Ocular motility; Conjunctiva, cornea, sclera 1620	Chicago Ophthalmological Society, November 21, 1949	1603
The Pinhole Test  CORRESPONDENCE  Sudan interior mission eye hospital Education of the Norwegian ophthalmologist  BOOK REVIEWS  The Truth about Your Eyes Transactions of the American Ophthalmological Society Ophthalmic Medicine Color Psychology and Color Therapy  ABSTRACTS  Anatomy, embryology, and comparative ophthalmology; General pathology, bacteriology, immunology; Vegetative physiology, biochemistry, pharmacology, toxicology; Physiologic optics, refraction, color vision; Diagnosis and therapy; Ocular motility; Conjunctiva, cornea, sclera  1620	Editorials	
CORRESPONDENCE  Sudan interior mission eye hospital Education of the Norwegian ophthalmologist  BOOK REVIEWS  The Truth about Your Eyes Transactions of the American Ophthalmological Society  Ophthalmic Medicine Color Psychology and Color Therapy  ABSTRACTS  Anatomy, embryology, and comparative ophthalmology; General pathology, bacteriology, immunology; Vegetative physiology, biochemistry, pharmacology, toxicology; Physiologic optics, refraction, color vision; Diagnosis and therapy; Ocular motility; Conjunctiva, cornea, sclera  1620		1610
Sudan interior mission eye hospital Education of the Norwegian ophthalmologist  BOOK REVIEWS  The Truth about Your Eyes Transactions of the American Ophthalmological Society 1616 Ophthalmic Medicine Color Psychology and Color Therapy  ABSTRACTS  Anatomy, embryology, and comparative ophthalmology; General pathology, bacteriology, immunology; Vegetative physiology, biochemistry, pharmacology, toxicology; Physiologic optics, refraction, color vision; Diagnosis and therapy; Ocular motility; Conjunctiva, cornea, sclera		
Education of the Norwegian ophthalmologist  BOOK REVIEWS  The Truth about Your Eyes		1614
The Truth about Your Eyes		1615
Transactions of the American Ophthalmological Society Ophthalmic Medicine Color Psychology and Color Therapy 1619 ABSTRACTS Anatomy, embryology, and comparative ophthalmology; General pathology, bacteriology, immunology; Vegetative physiology, biochemistry, pharmacology, toxicology; Physiologic optics, refraction, color vision; Diagnosis and therapy; Ocular motility; Conjunctiva, cornea, sclera 1620	BOOK REVIEWS	
Ophthalmic Medicine Color Psychology and Color Therapy  ABSTRACTS  Anatomy, embryology, and comparative ophthalmology; General pathology, bacteriology, immunology; Vegetative physiology, biochemistry, pharmacology, toxicology; Physiologic optics, refraction, color vision; Diagnosis and therapy; Ocular motility; Conjunctiva, cornea, sclera  1620		1616
Color Psychology and Color Therapy		1616
ABSTRACTS  Anatomy, embryology, and comparative ophthalmology; General pathology, bacteriology, immunology; Vegetative physiology, biochemistry, pharmacology, toxicology; Physiologic optics, refraction, color vision; Diagnosis and therapy; Ocular motility; Conjunctiva, cornea, sclera		
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immunology; Vegetative physiology, biochemistry, pharmacology, toxicology; Physiologic optics, refraction, color vision; Diagnosis and therapy; Ocular motility; Conjunctiva, cornea, sclera	Abstracts	
cornea, sclera	immunology; Vegetative physiology, biochemistry, pharmacology, toxicology; Physiologic	
		1620
	News Items	1664



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### THE RELATIONSHIP OF HETEROPHORIA TO DEPTH PERCEPTION IN AVIATION\*

WITH PARTICULAR REFERENCE TO THE WORK OF THE ROYAL CANADIAN AIR FORCE

#### PART I

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#### I. INTRODUCTION

The purpose of this thesis is to review the work to date on the relationship of heterophoria to depth perception as it affects pilot performance in aviation. Special emphasis will be placed on the investigations of the Royal Canadian Air Force, with which I am particularly familiar because of my wartime service.

The importance of the relationship of heterophoria to depth perception in the minds of the majority of experts is attested by the universal adoption of careful tests for heterophoria and rigid standards of acceptance by national licensing boards, air transportation systems, and the armed services. In an all-out war, such standards limit the number of men available for pilot duty.

The figures of Redway<sup>3</sup> in a recent study indicate that 2.5 percent of individuals have no stereopsis, and in another 20 percent it is deficient to some degree. These findings were confirmed by those of Davidson.<sup>2</sup> Benson,<sup>3</sup> on analyzing the causes of rejection of 500 candidates for flying training, found that 62.2 percent were rejected because of ocular defects. Disturbances of the ocular muscle balance were involved in little over a quarter

of these, Gore and Lawton,4 in another study, confirmed these findings.

In the Royal Canadian Air Force, for the period August, 1941, to October, 1944, 22,285 candidates out of a total of 102,536 were permanently rejected because of ocular defects.<sup>5</sup> Recruiting-center statistics relative to the frequency of disqualifying ocular muscle imbalances were not always dependable. However, in Section VII of this thesis quite dependable data are presented which indicate that 4.5 percent of a group of 4,327 aircrew candidates at recruiting center level were disqualified for pilot duty because of defective ocular muscle balance. Because of possible wastage of potential aircrew through having too strict visual requirements, and also because of scientific interest, the Royal Canadian Air Force felt it necessary to investigate the validity of these standards.

It should be mentioned here that, during the late war, the Royal Canadian Air Force in Canada was largely a training organization. A major portion of the British Commonwealth Air Training Plan was placed under the jurisdiction of the Royal Canadian Air Force. In Canada, 131,553° aircrew were trained.

Large numbers were directed into operational units of the Royal Air Force. Later, graduates also went into the operational

<sup>\*</sup> A thesis presented toward membership in the American Ophthalmological Society.

units of the Royal Canadian Air Force, the Royal Australian Air Force, and the Royal New Zealand Air Force. Hence, the medical branch of the Royal Canadian Air Force in Canada was very interested in the accurate selection of aircrew candidates.

It was interested also in reducing the standards of acceptance to the lowest possible level in order to make use of all potential aircrew and yet at the same time to

maintain efficiency and safety.

In the course of time, a great mass of data was collected and analyzed. The present thesis will present these data, and discuss the problem in its proper environment, which is that formed by the best knowledge of the time.

#### FACTORS IN SENSE OF DEPTH

In introduction, and as a background for further discussion, it might be well to review briefly what is known today of the factors that enter into the formation of the sense of depth.

The perception of depth has a very complex formation. It depends not only on purely sensory and physiologic matters, but it also involves a very complex psychologic integration process, which brings into action many factors, such as visual memory, logical analysis, and interpretation. Thus, experience plays a large part in its accurate formation, and psychologic aberrations may affect it.

The factors that enter into the development of the perception of depth may be divided into two groups:

The first has its basis mainly in ocular physiology inherent in the individual. Hence, some writers group these under the heading of "inherent factors," while others refer to them as "intrinsic factors." I prefer the term, "physiologic factors," as they involve the physiology of vision.

The second group has its basis in certain physical laws of light, and hence is referred to often as the "physical factors" group.<sup>7</sup> Others refer to it as the "extrinsic factors" group, and still others call it the "adjunctive" group. As will be seen later in this discussion, these factors are not adjunctive and, under certain conditions, may be the only factors operating. Many intellectual functions are involved in the interpretation of these factors, and hence more properly they may be called the "psycho-physical" group.

#### 1. Physiologic factors

a. Stereoscopic vision. This term properly is reserved for the third dimensional effect one obtains by integrating the two similar, but not identical, images received by the eyes. The lateral placement of the eyes in respect to the observed object produces a slight disparity of the retinal images. It is by an interpretation of this disparity that one obtains a sense of depth.

This stereoscopic function has effect only in relationship to objects having horizontal disparity. No sensation of depth is obtained from objects producing a purely vertical disparity. Diplopia merely is produced.

This is the essential situation, though Ogle<sup>10</sup> believes that there may be some crude form of spatial sense in vertical disparities which indicates heights above the horizontal. This is open to some doubt, however, in the minds of others.

The stereoscopic function usually is considered to be made up of two components:

- Binocular parallax, by which one eye views a group of objects from an aspect slightly to one side of that obtained by the other eye.
- ii. Physiologic diplopia—objects closer than the plane of the Hillebrand-Hering horopter<sup>11,12</sup> are seen in crossed diplopia, and objects farther away than this plane are seen in homonymous diplopia,
- b. Effort of accommodation. The nearer an object approaches, the more one must accommodate to see it clearly. Thus, from the effort of accommodation necessary to see an object clearly, one may determine where it is. Apparently the accuracy of this factor is

not great, as has been pointed out by Wundt, 13 Hillebrand, 11 Dixon, 14 Adler, 15 Walls, 16 and others.

On the other hand, Grant<sup>17</sup> concluded, as the result of his studies, that both accommodation and convergence play an equal and important role in determining the distance of near meaningful objects. His opinion appears to be a minority one, however.

Be this as it may, in landing an aircraft, judgment of depth and distance for objects nearer than 30 or 40 feet is not required. This is demonstrated clearly by a study of the standard procedure used by instructors in training student pilots how to land their aircraft. Hence, accommodation must play only an extremely small part in this action.

c. Effort of convergence. The nearer an object approaches, the more one must converge the visual axes in order to fix upon it with each eye. Thus, from the effort of convergence necessary to fix an object with each eye, one may obtain an idea of its position.

Again, since in landing an aircraft judgment of distances less than 30 or 40 feet is not required, convergence must play little part in this function. This concept is confirmed by a Valentine.<sup>18</sup> It is likely, also, that even at close range convergence plays only a small part in the perception of depth, because objects illuminated for only an instant (for periods well within the latent period of muscle) are well seen in their relative positions. Von Recklinghausen,<sup>19</sup> Aubert,<sup>20</sup> Helmholtz<sup>21</sup> have all pointed this out.

#### 2. PSYCHO-PHYSICAL FACTORS

a. Size. The nearer an object approaches the eye, the larger is the image it forms on the retina. The image size varies according to the formula:22

Size of image =

Distance of anterior focus from eye X Size of Object from anterior focus

Based upon one's experience of the relative size of objects, one then can determine the relative position of objects in space, The determination of depth by this factor alone may lead to faulty decisions, as the true size of objects may vary. Thus, very tall mountains, such as the Rockies, give the impression of being quite close, when in reality they may be very far off. This is particularly true if one's previous experience has had to do with the appearance of only small mountains.

On questioning pilots, it is apparent that this factor has only moderate value in landing an aircraft. However, one should note the opinion of Hargreaves, 20 who emphasizes its importance. Indeed, Mead<sup>24</sup> has pointed out that, under certain conditions, size may over-ride the depth effect produced by binocular parallax.

b. Motion parallax. As one moves past a landscape, near objects apparently move in an opposite direction, while more distant objects appear to move in the same direction. The relative speed of movement depends upon one's own speed, and upon the distance separating the objects from each other and from oneself. With experience, a person may develop a very accurate sense of depth by this method. Questioning of experienced pilots and pilot instructors indicates that this is an exceedingly important factor in the ability to land an aircraft accurately.

The importance of this factor was first emphasized by Brailey<sup>28</sup> in 1919. The relative movement of the runway and surrounding landscape past the aircraft fuse-lage, and the relative movement of various objects in the landscape, such as the runway stones, bushes, tufts of grass, hangars, and parked aircraft, are all very important clues. Helmholtz<sup>26</sup> pointed out that this factor was an exceedingly important one in the ability of one-eyed individuals to determine depth, an aspect which will be mentioned again.

c. Perspective. Under this heading are included such matters as:

 Aerial perspective; by which is meant the effect produced upon the clarity and definition of objects by the density of the atmosphere. The farther an object is away, the less distinct are its outlines, and the more blue-gray does it appear. One often is aware of an illusion produced by this factor. On very clear, dry days, distant objects are so distinct that one gets the impression that they are very close.

ii. The distribution of light and shade; for instance, the more prominent parts of an object are illuminated more brilliantly than the recesses.

 Overlapping contours; when one object obscures another, it must be in front of it.

iv. Geometric perspective; by this, parallel lines as they recede appear to converge and finally intersect at the horizon.

It is obvious in questioning pilots that perspective details are crude indications of depth. They form, as it were, background material only, in which the more important factors in depth perception determine the more exact details. Doesschate and Fischer,<sup>21</sup> in a very careful study, have amply proven this point.

On the basis of the above discussion, since certain factors have little importance in landing an aircraft, one may present a reduced classification of the factors entering into depth perception from the aviation aspect. It is as follows:

- 1. Physiologic factors
  - a. Stereopsis
    - (1) Binocular parallax
    - (2) Physiologic diplopia
- 2. Psycho-physical factors
  - a. Size
  - b. Motion parallax
  - c. Perspective (of limited importance)

It will be noted that all the physiologic factors in this condensed classification are binocular. That is, their perception depends upon accurate binocular vision. All the psycho-physical factors are monocular. That is, their accurate perception does not depend upon binocular vision, but is as accurate when viewed with one eye as with two. The one-eyed pilot apparently makes use of this latter group when landing his aircraft. As

has already been mentioned, Helmholtz<sup>28</sup> first pointed out the importance of the monocular factor—motion parallax.

#### PERCEPTION OF DEPTH

Both the monocular and the binocular factors enter into the formation of the perception of depth. There is no uniformity of opinion expressed in the literature regarding whether one group or the other is the dominant one. Duke-Elder<sup>28</sup> takes a middle-of-the-road attitude, feeling that one group works equally with the other, and on occasion may even correct illusions and errors produced by the other group. With this, Mead<sup>24</sup> is in essential agreement.

Howard<sup>29</sup> feels that the binocular factors are more important and accurate than the monocular factors. Howard, who was one of the pioneers in aviation ophthalmology, developed an instrument to measure depth perception in aviators. This instrument was so designed that if the test conditions were carefully controlled, binocular parallax was the main factor operating. Every attempt was made to reduce the effect of the monocular factors to a minimum.

Deyo, 20 using this instrument, compared the relative accuracy of monocular and binocular depth perception in a test group. She found that monocular depth perception was less accurate than the binocular type, as one might expect from the nature of the instrument.

It is not sound, as many authors have done, to quote Deyo's findings to support their belief in the superiority of binocular depth perception. Howard,<sup>29</sup> in discussing his instrument, stated that under ordinary conditions monocular depth perception was aided by many perspective elements.

Recently, Vernon<sup>31</sup> published the results of some careful experiments which indicated that monocular and binocular judgments of distance are equally accurate when there are many perspective or monocular clues in the field of vision. In a group studied by Litinskii<sup>32</sup> it was found that the majority

of the individuals tested had equally accurate binocular and monocular depth perception.

On the other hand, Spearman<sup>33</sup> stated that the most important clues to depth are monocular ones. Further, Spearman stated that the binocular factors give information only regarding relative position and not absolute distance. This view is supported by Lancaster,<sup>34</sup> but not by Howard.<sup>23</sup>

### RELATION OF DEPTH PERCEPTION TO LANDING AIRCRAFT

It should be noted also that the physiologic, or binocular, group has its greatest value at relatively close range. The accuracy of stereopsis is a function of the distance separating the eyes and the distance the observed objects are away from the plane passing through the eyes.34-36 The power to discriminate depth diminishes with the square of the distance between the objects and the eyes. Thus, the farther objects are away, the less accurately can they be placed by means of binocular factors. Stratton, 37 for instance, found the extreme range of his stereoscopic vision to be 580 meters, as calculated by means of a pseudoscope. In actuality, stereoscopic vision is probably only really efficient at much shorter distances than this-a point agreed to by Counsell.38 Thus, theoretically these factors have their greatest importance in "touching down" an aircraft, and not in making the approach to the landing strip.

In 1940, Walker<sup>30</sup> carried out an interesting study in which he was able to demonstrate, under the conditions of his experiment, the superiority of the binocular factors over the monocular factors with horizontally placed objects. These findings are interesting when evaluated in the light of Ogle's<sup>30</sup> experiments already mentioned, whereby the stereoscopic function is limited for practical purposes to horizontal disparity.

It is interesting to note that, from the point of view of the pilot making his approach for landing, objects in the landscape have both lateral and vertical components in their distribution. Thus, it would appear, aside from human variables, that whether the binocular or monocular factors predominate depends upon environmental conditions. The application of this concept was emphasized by Eliott.<sup>40</sup> As he has pointed out, under certain conditions binocular clues to depth may predominate, while under other conditions, monocular clues may predominate, thus influencing the interplay of the binocular and monocular factors.

In making landings upon unprepared landing fields, such as in forced landings, apparently binocular clues predominate. <sup>61</sup> Under other conditions, monocular clues play an equal part at least, and even may be dominant. This occurs when landing an aircraft on a prepared landing field. Here, the edge of the runway, hangars, parked aircraft, and such like, are strong monocular clues.

Under other conditions, monocular clues are the only ones. Thus, to aid landing an aircraft on still water or on newly-fallen snow, it is usual to place markers of known size at known intervals along the landing area. The size of a familiar object is a guide to the pilot in making his judgment of distance. Also, the angles subtended on the eye by the evenly spaced objects are a guide.

The same conditions arise when making a landing at night-time by the use of a flare-path. Livingston<sup>42</sup> has cited several interesting examples of this. Of course, if flood lights are used, the pilot also may have the aid of binocular clues.

An interesting study of the clues used by pilots in landing an aircraft has been made by McIntyre and Morson.<sup>43</sup> They emphasize the importance of the pilot fixing his gaze on points well in front of the aircraft when preparing to "touch down," and the importance of the apparent size and movement of objects outside the aircraft, such as tufts of grass.

#### VISUAL TASKS OF PILOT

To this point, the relation of depth perception to landing an aircraft only has been discussed. It is obvious that it plays a part in many other visual tasks of the pilot. These visual tasks have been classified by Byrnes<sup>41-46</sup> thus:

1. Estimation of attainment of flying speed on take-off (by speed of approaching objects).

Maintenance of minimum altitude until single engine speed is reached.

Maintenance of minimum altitude on bombing and strafing missions.

 Maintenance of proper position in formation flying.

5. Determination of when effective gunfire range has been reached.

Determination of distance from aircraft of shell bursts, to decide on effective evasive action.

Determination of distance from ground in landing, to decide when the plane should

be placed in landing attitude.

Not all these functions are important in peace-time flying. If, so far in the discussion of depth perception, the emphasis has been placed on the pilot's ability to land his aircraft, this would seem to be justified. The same elements in depth perception that affect his ability to land are also effective in his other functions. Also, his ability to land is more exactly determinable than are his other functions; and thus it forms the best center about which to build a study. The Royal Canadian Air Force investigations made use of this fact.

Also, many of the other pilot functions in which depth perception is used are aided by mechanical devices. Thus, in taking-off, pilots are trained to judge their speed by the air-speed indicator, and not by the speed of the approach of objects. There is good reason for this instruction—air-speed is the important thing in take-off, and not ground speed. Also, in the determination of gunfire range, the modern gun sight is the final court of appeal. It makes binocular depth perception unnecessary,

Byrnes<sup>44-46</sup> believes that binocular clues are exceedingly important when flying in

formation, and in the judgment of the position of approaching aircraft. He thinks this is particularly true of binocular parallax. It would be difficult to submit this statement to scientific verification.

In this respect, however, it is interesting to note Spearman's and Lancaster's opinions already expressed. They believe that binocular clues permit the determination only of relative distance. Other factors are required to determine absolute position. It would appear in any case that these functions require no more delicate perception of depth than does the ability to land an aircraft efficiently.

It is essential in assessing the importance of the various factors to remember always the complex nature of depth perception. This complexity is well indicated by the discussion just given. The position of binocular clues, in this hierarchy, was well epitomized by Woodworth<sup>47</sup> when he pointed out that binocular disparity is a stimulus, but depth effect is a response. Being a response, it is influenced by the psychologic status. Little study has been given to this aspect up to the present. It will be touched upon again in Section VII, in which the relationship of orthoptics to aviation is outlined.

Thus, it would seem that the use of binocular factors in landing an aircraft and other pilot duties is quite limited. And, by the same token, theoretically one would suppose that whether a man had or had not good binocular vision would not be an important matter in his success as a pilot. It was precisely these considerations that led to the investigations of existing visual standards by the Royal Canadian Air Force.

#### II. VISUAL STANDARDS IN AVIATION WITH RESPECT TO HETEROPHORIA AND DEPTH PERCEPTION

If one examines the visual standards set down by the armed services and by the closely related civilian licensing boards of various countries, one may see at once that there is a common denominator running through them all. They all insist that pilot candidates have stable binocular vision. To insure this, certain definite limitations are placed upon the amount of heterophoria that may be accepted. It is true that there are variations in the exact limitations made, and in the manner in which ocular muscle balance is tested. But nonetheless, it is obvious that they all belong to the same group.

From its foundation, in 1922, up to 1942,

With the cover test, not only is the amount of latent deviation noted, but also the manner in which the covered eye returns to alignment when uncovered. A rapid recovery of alignment is understood to signify good fusion, and a slow or jerky recovery is taken to indicate poor fusion. A failure to recover alignment means neglect, or suppression. Thus, by the type of recovery

TABLE 1
ROYAL AIR FORCE OCULAR MUSCLE BALANCE STANDARDS

.gp		Fit	Borderline	Temporarily Unfit	Unfit	
phor ox ro	Esophoria	0-2 p.d.	2-2.5 p.d.	2.5-3 p.d.	Over 3.5 p.d.	
Heterophoria Maddox rod	Exophoria	0-2 p.d.	2-2.5 p.d.	2.5-3 p.d.	Over 3.5 p.d.	
He	Hyperphoria	0-0.75 p.d.	0.75-1 p.d.	1-1.5 p.d.	Over 1.5 p.d.	
ion	Exophoric type	0-4	4-6	6-8	Over 8	
Fusion Bishop Harman	Esophoric type	0-5	5-6	6-8	Over 8	
Cover Test	Exophoric type	Slight latent di- vergence—rapid recovery	Latent divergence —slow recovery	Latent divergence —recovery with lag followed by jerky return	Latent wide diver- gence with no re- covery (neglect)	
	Esophoric type	Slight latent con- vergence—rapid recovery	Latent conver- gence with slow recovery	Latent conver- gence with slow recovery	Latent convergence with no recovery simulating conver- gent strabismus	
ular	Convergence (objective)	0-10 cm.	10–13 cm.	13-15 cm.	Over 15 cm.	
Binocular Gauge Test	Convergence (subjective)	This test is used to aid in assessing objective convergence. Usually the reading are slightly higher with subjective convergence.				

Note: p.d. = prism diopters.

the Royal Canadian Air Force followed the medical standards laid down by the Royal Air Force. This linkage between the two service standards became doubly strong with the inception of the British Commonwealth Air Training Plan in 1939. These standards are laid down in Air Publication 130<sup>18</sup> (referred to commonly as A.P 130).

In respect to the assessment of the ocular muscle balance, the standards are summarized in Table 1. It will be noted that there is a subjective test for heterophoria (the Maddox rod with muscle light at 20 feet) and an objective test (the cover test).

found, some measure of the state of binocular fusion is obtained.

By means of the Bishop Harman diaphragm test<sup>49</sup> a subjective crosscheck is made of this latter function. With this instrument, the candidate looks at a row of numbers on a card placed at the end of a rod 44 cm. from the eyes. Between the card and the eyes is a metal shield with a central aperture, through which the card can be viewed. By means of horizontally sliding shutters, the aperture can be made smaller from the temporal sides and the binocular overlap can be reduced gradually.

When a point is reached at which there is not enough overlap to stimulate binocular fusion, the eyes become dissociated, and take up their heterophoric position. The amount of shutter closure is read off a scale (the ocular poise scale), and is a measure of the stability of fusion, or what has been called "the desire for fusion." This reading is corrected for the interpupillary distance.

"the ocular muscle balance . . . must be normal."

In Canada, civilian licensing follows the standards laid down by A.P. 130. As has already been mentioned, up to 1942 these standards were also followed by the Royal Canadian Air Force. In 1942, somewhat more lenient and simplified standards in respect to ocular muscle balance were adopted

TABLE 2
ROYAL CANADIAN AIR FORCE OCULAR MUSCLE BALANCE STANDARDS 1942-48

a p		Fit	Borderline	Temporarily Fit and Unnt
Heterophoria Maddox rod	Exophoria	0-3.5 p.d.	3.5-4.5 p.d.	Over 5 p.d.
ladd	Esophoria	0-4.5 p.d.	4.5-6 p.d.	Over 6 p.d.
IN	Hyperphoria	0-1.5 p.d.	1.5-1.75 p.d.	Over 2 p.d.
op nan st	Exophoric type	0-3	3-6 (9 in special cases)	Over 9
Bishop Harman Test	Esophoric type	0-3	3-6 (9 in special cases)	Over 9
Cover Test	Exophoric type	Latent divergence with medium to rapid re- covery	Latent divergence with a short lag followed by jerky recovery	Latent divergence of a wide angle with no re- covery (neglect)
	Esophoric type	Latent convergence with medium to rapid recovery	Latent convergence with slow or jerky recovery	Latent convergence with no recovery— simulating internal strabismus
Binocular Gauge Test	Objective convergence (O.C.)	Up to 10 cm.	10-15 cm.	Over 15 cm.
	Subjective convergence (S.C.)	pend only on converge	ence power, but also up	only. Readings do not de- on p.d., the power of ac- tent. A single finding of a s under 18 cm. have little

Finally, convergence is tested objectively and subjectively.

It is stated in A.P. 130<sup>18</sup> that "the results of the various tests for ocular muscle balance should be considered together. The acceptance of candidates with border-line ocular muscle balance depends on their response to the tests for physical efficiency."

In A.P. 130 also are included the standards required of candidates for civilian pilot's license. It is stated merely that in candidates for A license (private pilot's license) and for B license (public transport)

by the Royal Canadian Air Force<sup>50</sup> (see table 2). The Royal Canadian Air Force studies, to be discussed later, were based on these standards.

As a result of these investigations, new standards have been adopted recently by which relatively lenient ocular muscle balance standards only are required of new trainees. Provision is made, however, for omitting these requirements in national emergency. In experienced personnel with good flying records, binocular vision is not required.<sup>31</sup> In the United States, Army,<sup>25</sup> Navy,<sup>52</sup> and commercial<sup>24-83</sup> standards require stable binocular vision. Thus, they have a similarity with those in other countries. The manner of testing, though, is somewhat different. <sup>44,84</sup> To qualify for pilot duty, the candidate must have no more than 10 prism diopters of esophoria, five prism diopters of exophoria, or one prism diopter of hyperphoria.

The presence of adequate reserve muscle power with which to control the heterophoria is insured by requiring that the candidate have no less than three prism diopters or more than 15 prism diopters of prism divergence. In any case, the prism divergence must equal the esophoria present. Also, there must be at least 40 prism diopters of prism convergence.

Depth perception is tested by means of the Howard-Dolman apparatus, 20, 55, 06 placed 20 feet from the candidate. An average error of 30 mm. is permitted in bringing the movable bar into alignment with the fixed one. This represents a parallactic angle of 10.3 seconds in an individual with an interpupillary distance of 64 mm.

Similar standards were in force in France<sup>57</sup> and Belgium<sup>58</sup> before World War II. In France<sup>59</sup> the standards since the war require an esophoria no more than 10 prism diopters, exophoria no more than five prism diopters, and hyperphoria no more than one prism diopter, both for military and commercial pilots.

In Sweden, the air service does not permit more than four degrees of lateral or one degree of vertical heterophoria. 60 The story is much the same in Spain. 61

In Germany, ea, ea up to the end of World War II, pilots were permitted to have six prism diopters of exophoria or esophoria at six meters. In cases of good depth perception, 10 prism diopters of lateral latent deviation were permitted. There was no official method of testing depth perception; it was left to the choice of the examiner.

In Russia<sup>64, 65</sup> no actual strabismus is per-

mitted. No more than two degrees (about four prism diopters) of horizontal latent deviation for distance vision, and not more than 10 degrees (about 20 prism diopters) of horizontal latent deviation for close vision is permitted. One degree only (about two prism diopters) of vertical latent deviation is permitted. Binocular vision is tested by means of the two-wire test, by which the candidate holds a wire in his right hand and tries to touch the end of a vertically fixed wire. While he makes his wire approach the fixed one, a frame is placed before his eyes in which are prisms base-out totalling 30 degrees. If his judgment is upset, the candidate has binocular vision. Sometimes, also, the Howard-Dolman apparatus is used.

Very similar requirements to those just mentioned were proposed recently as "recommended practices" at the International Conference on Civil Aviation held in Montreal, Canada, in January, 1947, under the auspices of the Provisional International Civil Aviation Organization. 66

By these "recommended practices," commercial and airline transport pilots are to have no more than one prism diopter of hyperphoria, 10 prism diopters of esophoria, and five prism diopters of exophoria. For student and private pilots, it is merely stated that "the ocular muscle balance must be satisfactory." 67

#### III. THE RELATIONSHIP OF HETEROPHORIA TO STEREOPSIS AND FLYING PERFORMANCE

The literature dealing with heterophoria in its relationship to depth perception and pilot duty goes back about 30 years to the latter part of the first World War. The original work upon which the present standards are based was carried out almost entirely in Great Britain and the United States. Since then, many papers have been published in several countries.

In reviewing these, one is struck by the large number that are inconsequential, and the number that repeat in almost direct quotation what has been said by others. Many present no data at A, but merely express opinions and are estantially commentaries. Many do not bear directly upon the theme of this thesis. For the bake of completeness, references are appeared (references 68 to 113 inclusive).

It is not necessary to review these papers in detail. Discussion were will be limited to the opinions of think who were, or are, leaders in the field, and to the findings of those who have carry I out original work.

In all these paper, the discussion pro and con has centered a fund the necessity of limiting heterophoric in pilots because of its possibly deleterious fect upon depth perception. The last wo always has been with those who support this contention. The present standards, as justified in Section II of this paper, well illustified this.

The attitude of the Royal Air Force up to and including the last war is expressed in paragraph 46 of for Publication 130,48 which still is the official manual for medical examination of pilog candidates. It states that "the ability of a bilot to land an aircraft successfully and concistently depends to a great extent on the presence of a normal ocular muscle balance."

One of the most prominent of the early workers in aviation ophthalmology was Clements, ophthalms specialist and later consultant in ophthalmology to the Royal Air Force. He first became interested in the effect of heterophoria on depth perception through a study on the relationship of visual defects to motor accidents. 114 He believed that stable binocular vision was essential in the ability to land an aircraft safely.

In support of this view he stated that 82 percent of pilots referred to him because of poor landing ability were successfully treated and returned to flying by ocular muscle training. 116 He also found a definite correlation between landing difficulties and the desire for fusion as measured with the Bishop Harman diaphragm test. Those with poor fusion were poor landers. He expanded his ideas further with later findings published in 1923. 116

Flack<sup>117</sup> confirmed Clements's opinion in regard to ocular muscle training. In reviewing this work in the Royal Air Force he noted that 104 officers with poor landings had received ocular muscle training, and of that number 73 had been traced at a later period. Of this latter number, 55 were able to resume their flying successfully.

Even at this early date not all British authorities were in agreement with this view. Brailey, 25, 118 in 1919, stated that he did not believe that heterophoria was related to the refinement of depth perception. He had found as many heterophorics among good landers as among bad landers. He stated further 25 that "in spite of statistics being overwhelmingly in favor of the importance of heterophoria, I am not able to persuade myself that there is not a good deal of fallacy both in the theory and in the results." On the contrary he stressed the importance of visual acuity, and the correction of refractive errors.

On the same occasion, Sir John Herbert Parsons<sup>119</sup> commented in regard to the studies both in England and the United States that "much more control is needed." In reference to the investigations of Brailey and Clements, he felt that they "ought to have been done against controls."

Although supporting the visual standards in general, Munro, 120 in 1923, again expressed the same criticism of the work on ocular muscle training when he said, "While real improvement has been effected in a number of cases of heterophoric bad landers, controlled statistics have not been obtained to show how far the improvement is due to the methods of eye training only, or as to how long improvement is maintained."

Greene, in 1919,<sup>121</sup> in discussing heterophoria and muscle training said that he did not take much interest in ocular muscle balance as he felt that men with one eye could do most things required. From the Royal Flying Corps there had been sent to him those who had crashed several times, and he usually found that there was nothing wrong with their vision. Some did well after a rest.

In 1918, Anderson<sup>128</sup> analyzed 58 crashes. He found that an error in judgment on the pilot's part occurred in 42 cases. Four of these latter occurred on take-off and 38 on landing. In comment he stated that "it is difficult to account for these errors in judgment. In some cases it may be due to underinstruction. In other cases, even after prolonged instruction, the pupil may misjudge distances, and on examination one occasionally finds that his standard of vision is below normal, but on the other hand, he may be found physically fit, with normal vision and balancing power."

In 1926, Clements<sup>183</sup> published his findings on a group of 72 pilot trainees who "ceased training" because of poor landings. In this group he found no cases of orthophoria, At the same time he studied 397 civilian pilots who were known to be satisfactory flyers. Of these latter, he found that 97.5 percent were orthophoric. In the light of present knowledge regarding the incidence of orthophoria, these figures are difficult to accept. In a general group of individuals, orthophoria is the exception rather than the rule.

Further support is given to this by Hoffman's figures. 134 Among 1,822 German pilots he found that only 9.4 percent were orthophoric. These latter findings are supported by those of Thorne 134 to be mentioned later in more detail. The findings of the Royal Canadian Air Force to be dealt with in Section V of this thesis also support this latter attitude.

Thus, Clements's opinion that heterophoria produces errors in depth perception, which was based largely upon the empirical results of ocular muscle training, became the center of some controversy. However, it was supported by certain American authors.

Wilmer, 126 in 1918, concluded that "we may safely say that ocular muscle balance is one of the most important points to be considered in aviation." Later, in 1919, 126 he somewhat modified this viewpoint by stating he believed that under certain conditions experienced one-eyed pilots might be permitted to fly.

Howard<sup>10</sup> in the same year, basing his remarks on a study of 106 case reports, stated that stereoscopic vision depends upon visual acuity, equality of visual acuity, normal ocular muscle balance, the interpupillary distance, and probably some innate and acquired ability.

Wilmer and Berens, 127 in 1920, reported on the successful use of extraocular muscle training with the American Expeditionary Force in France. Berens, 128 in 1923, reported material suggesting the importance of stable ocular muscle balance. A study of American aces, and of successful French and British pilots, showed the uniform presence of exceptionally good visual acuity and good stereoscopic vision. This last paper 128 is a valuable contribution, as it gives a complete summary of the literature up to that time.

In the United States, however, this point of view did not go unchallenged. Lancaster,34 in 1919, said that it had been stated freely by various writers that stereoscopic vision was exceedingly important, if not indispensable to the flyer. This seemed doubtful to him for these reasons: "(1) Because it is not uncommon to meet a flyer who lacks stereoscopic vision, and yet who maintains-and justly so-that he makes good landings; (2) stereoscopic vision enables one to estimate relative distances with great accuracy when objects are near one, but the power to discriminate diminishes with the square of the distance, and at the comparatively long range at which the flyer works, this means of judging distance is surpassed by other methods of judging."

It is interesting to note in respect to the second contention that Spearman, 33 in England in the same year, stated that stereopsis merely denotes relative position and not absolute position. Howard did not entirely agree, however.

Verhoeff<sup>129</sup> in discussing Howard's<sup>29</sup> paper dealing with his test for depth perception stated: "It seems to me that it is questionable whether this test will decide the ability of the aviator to estimate distance. We want to know with what accuracy he judges

distance by binocular vision, not alone the slightest distance that he can recognize. No one, as far as I know, has attacked this problem."

Franklin, 180 in the same year, stated his belief that the sense of depth was neither essentially ocular nor tactile nor muscular, but a psychic complex growing from these three elements. Dudley 181 after studying several specific cases came to the conclusion that "in all probability there is little relationship between stereoscopic vision and the ocular muscle balance."

From the foregoing, the point that heterophoria affects depth perception and adversely influences the pilot's ability to land his aircraft would seem to be far from agreed to by all workers. Apparently those in favor of the view had the greater influence. Their opinions culminated in the development of international visual standards, by which the amount of acceptable ocular muscle imbalance was limited. These standards were laid down at the Peace Convention held in 1919.<sup>132</sup>

Following this, the standards were revised from time to time, and finally, at Rome, in October, 1927, minimal standards of a similar nature were agreed on for international use by the medical subcommittee of the International Commission for Air Navigation, 133 This stand again has been reiterated by the "recommended practices" of the Provisional International Civil Aviation Organization, as has already been mentioned in Section II.87

Since 1927, a great number of papers pro and con have been published in several countries, and, as has been mentioned, many of them add little to the picture. In Great Britain, the work of Clements was followed by that of Livingston, who was his successor in the Royal Air Force.

Livingston's attitude to the question was changeable. In 1934,<sup>154</sup> he stated that aberrations outside the ocular muscle standards of Air Publication 130<sup>18</sup> almost invariably led to errors in judgment of distance in landing. In 1935<sup>135</sup> he noted that "there is need for a

thorough revision of the whole subject," as he said the ocular muscle standards were based primarily on empirical grounds by Clements during the first World War. He said further that "it is not necessary to have such an amazingly good muscle balance in order to fly aeroplanes." In 1937<sup>136</sup> he wrote that symptomless heterophoria was better left alone. In 1937 he presented<sup>137</sup> examples of successful monocular and uniocular pilots, and stated his belief that the monocular condition does not affect flying performance aside from the risk attendant to the reduced field of vision.

Later, in 1939,<sup>138</sup> he stated that "there is not the slightest doubt that the basic cause in very many cases of pilots who cannot carry out landings on aerodromes or aircraft carriers is an ocular muscle imbalance." Again in 1940,<sup>139</sup> while admitting the complexity of depth perception, he stated that "heterophoria can exert great influence upon the landing of aircraft."

Ballantyne, 100 in 1940, could not fully agree with a strict attitude in this regard, but felt that a "notable degree of heterophoria is compatible with good duction power and perfect stereoscopic vision." Livingston 141 in 1944 presented figures showing the value of orthoptic training in salvaging pilots having landing difficulties. As with Clements's work, the study was uncontrolled, and very incomplete data were presented.

A somewhat less equivocal, though no less confusing, attitude than that taken by Livingston has been expressed by J. C. Neely, who recently succeeded the former as consultant in ophthalmology to the Royal Air Force. He stated in 1947,142 "It has long been recognized by the Royal Air Force that ocular muscle balance and depth perception have little, if any, effect on the ability to learn to fly (see paragraph 46 of Air Publication 130, as mentioned earlier in this part). When, however, fatigue, mental stress, and physical debility are brought into the picture, those men whose ocular muscle balance is defective are less able adequately to meet the demands made upon them. There is no

relationship between a compensated heterophoria and depth perception, nor is there in a heterophoria artificially produced with prisms, in which binocular single vision can be maintained."

This statement appears to contain some mutually conflicting concepts. If heterophoria and depth perception (presumably stereopsis) have no effect on the ability to learn to fly, and compensated heterophoria or artificially produced heterophoria have no relation to depth perception, how can one relate defects in ocular muscle balance to the ability to do a job as pilot?

It is an interesting point in relation to these papers published by the English authors from 1919 on that none of them present well-controlled studies or sufficient data to support the claims made. It is true also that the many American studies do not present fundamental data relating heterophoria to flying performance. In the United States the best work has been on the deleterious effect of anoxia and fatigue on heterophoria and depth perception. It is from these latter studies that the soundest scientific support has come for the maintenance of the present standards. These studies will be dealt with separately in Section IV.

In 1926, Bauer<sup>143</sup> in his textbook, Aviation Medicine, expressed his opinion in support of the pioneer work of Clements and Wilmer.

In 1930, Thorne<sup>144</sup> maintained that heterophoria was the commonest functional defect encountered in the examination of rated and prospective flyers, and reduced power of convergence was the second most common defect. In a study of 500 pilot candidates he found 244 with horizontal imbalance and 132 with vertical imbalance. Of the 500 in the original group, 348, or 69.7 percent, were "ceased training" because of lack of progress. Of the 244 exhibiting horizontal imbalance, 72.5 percent were eliminated. Thus, this study, unlike many others, had a control series for comparison.

Thorne felt that whether or not heterophoria played a part in the elimination of these students was open to discussion. In 1938, he<sup>145</sup> reviewed the matter of depth perception and stated that he felt defects in it were due to many factors, the most important of which were—defective vision, errors of refraction, accommodation-convergence imbalance, imbalance of ocular muscles, and asymmetry of the ocular images.

Spearman, 106 in 1940, however, was more definite, and concluded that heterophoria influenced the judgment of distance. Millis, 147 in 1944, further supported this point of view.

As pointed out in Section I, Deyo, on the basis of experiments with the Howard-Dolman test, showed that monocular depth perception was only 20 percent as accurate as binocular depth perception, As already stated, these findings are applicable only to her test conditions, and are not necessarily applicable to the general picture. However, as in England, not all workers agreed with the standards.

In 1924, Doyne<sup>148</sup> stated his belief that a one-eyed man, after he has learned to judge distance with one eye, often may be less dangerous than two-eyed individuals in whom binocular vision is unreliable. Davis, <sup>149</sup> in 1927, supported the belief in the importance of orthophoria.

Stitt, 150 in 1929, stated that "the specialists at Pensacola have failed to note any superiority in students who just pass various eye tests with those who have little or no defect." His opinion is supported by the study of Ickstadt 151 carried out in 1929, Ickstadt examined 476 cadet pilots in the United States Navy, and found that the heterophoria present, which was within official standards, could not be correlated with flying performance.

Berens, 192 in 1932, published a most comprehensive paper reviewing the status of the visual standards up to that time. His attitude was that, other things being equal, stereopsis was a valuable asset for a pilot, but he felt that it was not necessarily essential.

Jarman,183 in a paper published in 1932, discussed the methods by which one-eyed

pilots successfully fly, and cited several cases of successful monocular pilots. He emphasized the importance of motion or monocular parallax, an aspect discussed in Section I.

Bean,<sup>184</sup> in 1941, while in general supporting the present standards, cited the case of a pilot with 5,000 hours flying time in 16 years of flying, who never made a good showing with the depth-perception test (Howard-Dolman test). Davidson,<sup>2</sup> in 1942, also expressed the opinion that minor heterophoria seems to have no adverse influence on depth perception. Graham,<sup>115</sup> in 1943, felt that under many circumstances monocular vision may be sufficient.

It is interesting in regard to the one-eyed pilot that Wurdeman, 186 as a result of a study with the Ransom-Pickard tests, found that in approximately a year after the loss of one eye, a certain degree of depth perception is acquired. In a long-standing monocular individual, it is also present. In this study, such people obtained a score of 50 to 75 hits out of 100 with this test. Those with normal stereoscopic vision obtained perfect scores.

In other countries, too, the matter of the relationship of heterophoria to depth perception and flying performance was the subject of some controversy. Much of the work carried out on continental Europe was more carefully done than similar studies in England and America.

In Germany, the earliest work was that of Halben, 187 1914, who stated his belief that good binocular vision was valuable, but nevertheless he felt that a one-eyed pilot with experience is better than a two-eyed one with unreliable eyes. Indeed, he believed that binocular parallax plays little part in depth perception at the great distances at which judgment must be made in landing an aircraft. The complete train of thought in Germany cannot be followed as there is a great gap in the published literature immediately after World War I.

The next most important study that can be found is that of Pol, 100 In 1930 he reported a study of 254 air personnel in which he found that there was an appreciable disturbance of depth perception when heterophoria was present. However, the investigations of Velhagen, 100 in 1937, at the Research Institute for Aviation Medicine in Berlin led him to conclude that "new fundamental investigations into the relationship of heterophoria to depth perception at ground levels and at high altitudes are very necessary." The same author 100 expressed much the same idea in an earlier study published in 1936.

In 1940 the influence of heterophoria upon the acuity of stereopsis in 500 young navy personnel was studied in detail by Junker. 181 The men were all 19 to 20 years of age, with 20/20 or better vision, and with no more than 1.5 prism diopters of hyperphoria; esophoria and exophoria occurred in various individuals up to 10 prism diopters. He concluded that no relationship exists between the degree of heterophoria, range of fusion, and the acuity of stereopsis.

Jongbloed, 102 in Holland, studied the effect on the ability of experienced pilots to land an aircraft produced by covering one eye. He found that they did quite well in spite of this handicap.

In Russia, the story is very difficult to follow, as most of the material has not been published in available journals. As already pointed out, according to Vishnevsky,64 stable binocular vision and good depth perception are required of all pilots. Litinskii, who did some of the earliest published work in Russia, stated in 1936163 that ocular muscle imbalance lowered the acuity of depth perception. However, in 1938,164 he revised this opinion after studying 100 candidates for pilot duty. As a result of this study, he concluded that the acuity and rapidity of depth perception ran parallel, and that the latter was not different in cases of orthophoria and heterophoria.

In France, starting with Cantonnet, 168, 160 the importance of stable binocular vision has been emphasized. Cantonnet felt that stere-opsis is important from the point of view of depth perception and flying performance.

Onfray<sup>167</sup> supported this contention, Later authors, of whom Duguet is the most prominent,<sup>66, 168</sup> however, have supported the standards mainly because of the deleterious effect of anoxia.

In South America, D'Oliveira Esteves, 169 in 1939, published a study of the relationship of stereopsis to flying performance as measured with a special instrument of his own design. He felt that errors in stereoscopic vision are not sufficient reason for rejection, providing the pilot candidate is well compensated. He believed that pilot candidates should be given six hours of flight instruction. If, after this period, the candidate's conception of depth is not corrected, he should be rejected, as he will not be educable in "space sense" sufficiently to permit flight.

In the Australian literature, there are several references to this subject. Most of the work there has dealt with it from an orthoptic approach. Some of the earliest work was carried out by Counsell,80 1940. He expressed some doubt that accurate stereopsis was very essential in the type of depth perception involved in landing an aircraft. He studied 49 random cases from the Royal Australian Air Force with ocular muscle balance near the permissible limits. He found no correlation between muscle balance, amplitude of fusion, and stereoscopic perception, thus confirming the findings of Junker<sup>161</sup> already mentioned. He confirmed this opinion in a paper published in 1941 in which he reviewed the literature dealing with the application of orthoptics to heterophoria and faulty depth perception in aviation. 170

Anderson, <sup>171</sup> in 1940, however, felt that accurate stereoscopic vision was exceedingly important. In 1941, Anderson <sup>172</sup> published the results of his investigations involving 300 pupils at Elementary Flying School. He rated the men on the basis of acuity of stereopsis, and ocular muscle balance—taking particular notice of the controlled convergence. He found a relationship between acuity of stereopsis and ocular muscle bal-

ance, which he called "striking." In analyzing his figures, it is true a relationship between the two can be demonstrated, but it is far from absolute.

Similarly, Anderson found that the time required to fly solo and the early flying performance were influenced by the excellence of stereopsis and controlled convergence. Again, on analyzing his figures, a relationship can be found, but it is far from absolute. The difference in performance between those with the best stereopsis and those with the worst was not uniform—many with poor stereopsis did very well, and vice versa. On the whole, it might be said that there was a relationship but it was slight.

In the same year, Willoughby 173 reported another study involving 318 pilots, She could find no evident relationship between range of convergence, voluntary convergence, and acuity of stereopsis on the one hand, and the ability to learn to fly on the other. She concluded that "the evidence produced by these figures is in no way consistent or conclusive that the state of binocular vision affects the trainee in his ability to learn to fly." In commenting upon Willoughby's work, with which he had been associated, Tostevin<sup>174</sup> stated that "the number of cases in which ocular defects are the primary cause of failure of a pupil trainee are negligible."

Travers<sup>179</sup> in discussing Willoughby's paper reported his findings in a similar study. His results suggested that "fusion amplitude had no relation to flying ability." However, the same author<sup>176</sup> in 1943, when discussing ocular muscle balance and flying performance, stated that "it is most important for pilots to have good muscle balance."

This might be the appropriate time to summarize the findings of the various workers in this most difficult field. The material presented in Section I indicated that depth perception is an exceedingly complex function, being composed of perceptual, environmental, and psychologic elements. It was pointed out that there are few or no occasions on which the pilot is dependent upon binocular clues. Usually, monocular clues are equally important, or even dominant.

The subject matter of the literature reviewed in the present section has approached the problem another way. As pointed out, many of the conclusions drawn by various

authors are unreliable. The mass of trustworthy evidence indicates that heterophoria, within quite wide limits at least, has a negligible influence on the acuity of stereopsis and on flying performance.

(To be continued)

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#### THE USE OF INTRAVENOUS NOVOCAIN IN OPHTHALMOLOGY\*

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Novocain has been extensively used as a local anesthetic and in the therapeusis of pain since 1905. Its introduction into the system through the intravenous route was advised by Bier¹ in 1908 as an anesthetic procedure. Progress in the modes of intravenous novocain techniques lapsed until the recent war when Leriche,² in 1941, described a method of intravenous novocain injection to ease pain in the lower extremities. Tovell³ suggested its use as an analgesic for battle casualties. Berthelmy⁴ and Hazard⁵ reported its use for frostbite, sprains, and fractures.

Prior to this time Leriche and Fontaine<sup>6</sup> had shown that the injection could be given safely, but had very little opportunity to try the procedure on a large number of patients. In this country, Lewy<sup>†</sup> tried a small injection of but 7 to 10 cc. of one-percent procaine, and reported that the injection reduced the intensity of the tinnitus in his patient. More recently, Allen<sup>®</sup> reported good results in the treatment of painful traumatic conditions.

Other American workers reported on a variety of unrelated conditions. Of pertinent interest is the report from State and Wangensteen<sup>9</sup> and that of Dressler and Dwork.<sup>10</sup> They all noted a beneficial effect in certain known allergic diseases.

The most extensive work, however, emanated from Graubard at the New York Post Graduate Medical School and Hospital. In 1948, Graubard and his associates reported on 1,954 intravenous infusions. The cases included painful fractures, arthritis, vascular diseases, and thrombophlebitis. The procedure was judged to be safe and a valuable adjunct in the management of selected traumatic, inflammatory, and spastic conditions.

Although the use of intravenous novocain

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has been thoroughly investigated and found to be satisfactory by the orthopedists, little has been reported thus far concerning its use in ophthalmology. Yet, a study of the chemistry and the physiology involved makes it seem likely that some benefits may also be gained in the therapeusis of certain ocular disorders.

Its use in ophthalmology, though infrequent, is not entirely new. Lorofitt reported its use in the treatment of visual disorders from tryparsamide. Gerbosi and Burgio<sup>12</sup> used it in the treatment of amaurosis following streptomycin therapy. Esente13 reported its use in the treatment of glaucoma. He concluded that the tension drops after 2 to 3 hours following a small injection of 1- or 2percent novocain solution. Acute glaucomas responded better than the more chronic types. Schiff-Wertheimer and Gaillard14 reported good results when novocain was used in the treatment of branch retinal vein occlusion, if used early enough. The only reported work thus far in this country is that of Givner and Graubard<sup>15</sup> who found no reduction in intraocular pressure in either normal individuals or in a series of glaucomatous patients.

One of us (E. E. G.) 10 has reported a dramatic response following its use in a case of amblyopia following massive hemorrhage after thyroidectomy but, in addition to the administration of novocain, a stellateganglion block was done.

#### PHYSIOLOGY

Outside of the field of ophthalmology, all research workers have based the beneficial results obtained with novocain upon the principle that within injured or inflamed areas, a condition of increased vascular permeability exists. This localized tissue condition is the result of a reflex action causing vasospasm and thereby tissue hypoxia. This increased capillary permeability allows the passage of fluid elements into the surrounding tissues and edema is the final result.

When novocain is given intravenously the

drug accumulates at the site of the inflammation, that is, the region showing an increased capillary permeability, and exerts a definite selective action to break up the reflex pattern, and thereby relieves the vasospasm. The effects described represent mainly a local action of novocain, which diffuses through abnormally increased permeable capillaries to anesthetize peripheral nerve endings. In view of this physiologic action, it would appear likely that analogous morbid situations within the eye would also respond in like fashion.

In recent years there has been a tendency to explain a great number of pathologic conditions within the eye as being due to vaso-spasm. Duggan<sup>17</sup> has been the leading exponent of the theory that focal infections of the eye may be due to vascular reflexes leading to liberation of histanine at points distant from the original focus of infection. He has placed great stress on the vascular basis of allergy, and has rationalized the physio-pathology in a host of unrelated ocular disorders.

However, the morbid changes in the tissue, as explained in the Duggan theory as being due to the liberation of histamine which causes arteriolar constriction, a dilatation and increased permeability of the capillaries, and consequently a tissue anoxia and finally edema, are in no way different from the reflex pattern caused by painful stimuli to an inflamed or injured articular joint.

It is on this basis that intravenous novocain offers a broad unexplored field of study. The practical value would appear to exist actually for two conditions, namely, to relieve arteriolar constriction, and secondarily to relieve pain. It is entirely possible of course, that by virtue of simply relieving severe pain, the reflex pain stimuli may become abolished, favoring vasodilatation by removing the vasoconstricting influences.

There is some scientific controversy regarding the specific physiologic action of the injected novocain. When injected intrave-

nously, the novocain is hydrolyzed into paraaminobenzoic acid and into diethylaminoethanol. The former is removed from the blood in less than an hour. Graubard and Givner15 noted the similarity of the structural formula between benadryl, choline, and diethylaminoethanol, and compared the mode of action with benadryl at the capillary bed, that is, a competition between histamine and diethylaminoethanol for a given site of action. The latter has a anticholinesterase action. However, the action on the acetylcholine-cholinesterase system is not quite certain. The predominant evidence indicated inhibition of acetylcholine.

Frommel19 tries to explain the paradox of clinical action by stating that there is an antiadrenalin action which is greater than the anti-acetylcholine one and, therefore, the results due to sympathetic prevalence are thus

explainable.

Sollmann<sup>20</sup> states that the pupil is dilated and Hirschfelder (1915) is credited with the proof that the retinal vessels are constricted. Orth,21 when looking up these original sources, finds that the evidence is not direct and that procaine is not mentioned.

Givner18 found the intravenous injection of novocain to be of no beneficial effect in reduction of intraocular pressure. The 10 cases of glaucoma included six of the chronic, simplex type and four of the old secondary type of glaucomas. In no instance could one determine that an acute vasoconstriction had occurred resulting in exudation or undue swelling of the ciliary body. Unless the latter features are present, there seems to be little rationale for the use of intravenous injection in the treatment of glaucoma.

Acute congestive glaucoma, on the other hand, presents the pathologic picture of arteriolar constriction with dilatation and increased permeability of capillaries and resultant edema. On theoretical grounds this would be the only condition likely to be affected by intravenous novocain. If nothing else, the analgesic effect of the infusion would be somewhat superior to the effects of morphine. This is in agreement with the findings of Esente18 who demonstrated a reduction in intraocular pressure in his acute glaucomas, but very little reduction when used in the long-standing cases.

Perhaps the work of Schmerl and Steinberg,22 regarding the role of the ciliary and superior cervical ganglia in ocular tension, may offer some explanation and rationale in future investigation, Graubard, 18, 18 quoting Musicant, claims that procaine administered intravenously has been found to be eight times more concentrated in inflamed tissues than in normal tissues. Schmerl concludes that the ciliary ganglion conveys fibers of essentially parasympathetic nature and produces vascular dilatation with a consequent increase in ocular tension. If these fibers are affected by the novocain, a resultant decrease in intraocular pressure can be anticipated.

As to benefits obtained in cases of retinal vein occlusion. Schiff-Wertheimer<sup>14</sup> obtained uncertain results when the central retinal vein was occluded but reported satisfactory results in branch obstructions if they were treated early enough. Givner18 obtained no effects in occlusion of retinal arteries nor in five cases of thromboses of retinal vein branches. The cases to be reported herein were treated with intravenous novocain on the basis that the theoretical and clinical picture suggested the possibility of acute vasoconstriction.

#### TECHNIQUE OF INTRAVENOUS THERAPY

The method advocated by Graubard28 and his associates was used. Five cc. of 20-percent solution (one gm.) of procaine hydrochloride is added to 1,000 cc. of isotonic saline solution. The material is given intravenously using the drop method and adjusted so that the rate of flow is between 60 and 75 drops per minute. Given at this rate, the procaine is not anesthetic but analgesic. The procaine solution given slowly is harmless because it is destroyed within a few minutes after entering the blood stream.

#### REACTIONS AND TOXIC SYMPTOMS

There is no definite ratio between the toxicity of procaine and cocaine, since this depends entirely on the rate with which they enter the circulation. Procaine is rapidly destroyed in the liver, and while in the blood circulation it is hydrolyzed to para-aminobenzoic acid and diethylaminoethanol,

Investigators have emphasized that sensitivity may be tested by injecting a drop of two-percent solution intradermally and waiting at least 15 minutes for the reaction. If the result is negative or doubtful, a drop can be instilled in one eye for further verification. If symptoms do develop, the rapid destruction of procaine in the liver results in immediate clearing of symptoms when the administration is interrupted.

Graubard18 has reported that in about 5 to 7 minutes after administration the patient feels a comfortable sense of warmth with relaxation, light-headedness, occasional lacrimation, slurred speech, and less frequently a metallic taste. The metallic taste may indicate the first sign of toxicity and the rate of instillation should be reduced slightly. Some euphoria is experienced by almost all of the patients.

Relief of pain and spasm is noticed within a few minutes of administration and this is continued generally for a few hours to several days. Nausea and tingling sensations of the extremities may be experienced plus a feeling of general numbness. There appears to be no significant effects on the pulse, blood pressure, or respiration.

Signs of overstimulation of the central nervous system by convulsions is the most serious complication. This can be controlled by cessation of administration and can be prevented to a great extent by the administration of a barbiturate beforehand or by giving sodium pentothal intravenously immediately. Of course, the administration of the drug should be stopped immediately

upon development of central nervous-system

Some generalized allergic reactions have been seen and they are characterized by swelling and itching of the hands and arms.

#### CASE REPORTS

CASE I

A 62-year-old man presented himself with a bilateral iridocyclitis. Vision was: R.E., counting fingers at two feet; L.E., counting fingers at eight feet. The right eye did not correct with lenses; the left, corrected to 20/50. He had several occurrences of red eyes in the past two years. Tension was: R.E., 32 mm. Hg (Schiøtz); L.E., 18 mm. Hg.

Slitlamp and vitreous studies were consistent with the iridocyclitis. The anterior chambers were filled with a heavy gelatinous media with evidence of no thermal circulation due to the heavy aqueous. No posterior synechias were present, the anterior lens capsule showed many deposits and the vitreous was so cloudy in both eyes, the fundus was not visible. A search for foci of infection was started and none were found.

Cycloplegics reduced the tension of the right eye to 20 mm. Hg. Penicillin and extensive intravenous typhoid therapy was started. The condition became progressively worse, therefore the typhoid therapy was discontinued. Severe bilateral blepharospasm and photophobia with browache and headache were

Intravenous novocain (one gm. in 500 cc. of saline) was started as described. In eight minutes the patient experienced complete relief from pain, blepharospasm, photophobia, and headache. He opened his eyes and became perfectly comfortable for the first time in three weeks. The entire 500 cc. was given intravenously. He spent a comfortable night with no sedatives or analgesics.

Twenty-four hours later he still had no blepharospasm or discomfort. The eyes were open. No browache or headache was experienced. The eyes appeared less injected and he had discarded his smoked glasses The photophobia and lacrimation had disappeared. The patient stated he could see better. Forty-eight hours later the same relief of symptoms persisted. About 72 hours later the symptoms of blepharospasm and burning began to return. He had experienced complete relief for 60 hours. Visual acuity had not changed thus far and slitlamp examination showed no change in the anterior segment. Intravenous administration of 100 mg. of novocain in 20 cc. of saline was given in a period of three minutes. Complete relief of symptoms in seven minutes was again experienced by the patient; 24 hours later relief of symptoms persisted and the patient stated he saw better.

Visual acuity of the left eye increased two lines. There was no change in the vitreous but the anterior chamber showed a great decrease of the amount of flare and a thermal circulation was noted for the first time. The eyes appeared whiter. The relief of symptoms persisted for 96 hours after which time a slight blepharospasm again reappeared.

At this time, one gm. of novocain in 500 cc. of saline was again administered intravenously which relieved the symptoms in a few minutes; 48 hours later the flare in the anterior chamber was almost all gone and the eyes were almost white.

Visual acuity returned to; R.E., 20/40; L.E., 20/40, corrected. The vitreous began clearing and the keratic precipitates were disappearing. Four days later the eyes remained about the same; no

symptoms were present.

The patient was discharged from the hospital and was seen two weeks later. The eyes were white, the vitreous was clear. The fundus was normal but a few cells were still present in the aqueous of each chamber. Almost all of the keratic precipitates had disappeared. Visual acuity was 20/40, O.U., corrected.

One month later the eyes were completely white. There was no discomfort, no flare in the anterior chamber, and the vitreous remainded clear. The fundus showed marked arteriosclerotic changes. Visual acuity was 20/30, O.U., corrected.

#### COMMENT

The diagnosis made was plastic iridocyclitis. The extreme pain and blepharospasm were quickly relieved. The clinical picture improved concomitantly. The beneficial effect was presumed to be due to relief of angiospasm and pain.

## CASE 2

A 33-year-old white man was seen in the outpatient department and gave the following history:

Three hours previously he experienced a blinding flash of light in his right eye for no apparent reason. The vision dropped immediately to light perception only. Two hours later the vision began to improve slowly. We saw him three hours after the initial symptoms. The vision was: R.E., 20/50; L.E., 20/20. The right visual acuity improved to 20/40 with a pinhole. Tensions were normal; externally the eyes were negative. No diplopia was present. Media were clear. The fundus of the right eye showed a macular edema and the vessels appeared normal.

A 1/1,000 white central field showed a concentric contraction of the field of the right eye to seven degrees. A 5/1,000 white target gave a normal full field. A 10/1,000 blue and red field showed a con-

centric contraction.

A diagnosis of angiospastic retinitis was made. He did not wish to be admitted to the hospital but returned 24 hours later for admittance and treatment. One gm. of intravenous novocain was given; 24 hours later there was no change of the fundus of the right eye but visual acuity improved to 20/25-3, uncorrected, and the field increased to

Vision of the right eye, 24 hours later was 20/20—3, uncorrected, and the fields increased to 24 degrees. He stated that a slight film persisted over his right eye. The fundus showed less macular edema. One more gm. of novocain was given and five hours later the patient stated that the film over the right eye had completely disappeared. The next three days showed gradual improvement and return of full fields with all isopters. The mascular edema had disappeared and visual acuity returned to 20/20, O.U., uncorrected. At no time was his blood pressure raised.

#### COMMENT

The diagnosis made was angiospastic retinopathy. This case was ideally suited to the use of intravenous novocain, and benefited immediately from the relief of angiospasm.

#### CASE 3

A 27-year-old white man presented himself with the complaint of blurring of vision of the left eye for three weeks.

'Examination revealed visual acuity: R.E., counting fingers at two feet; L.E., 20/40, with no improvement with pinhole or refraction. The right eye was injured in childhood with resultant vision as above as long as he could remember.

The fundus of the right eye showed macular changes and evidence of a choroidal tear between the macula and the disc. Fundus findings in the left eye were slight swelling of the disc, with edema and striations about the disc border. Veins were slightly dilated. There was a slight pigmentary disturbance of the macula.

Field studies of the left eye showed a concentric contraction to five degrees with a 5/1,000 white test object. The contraction for red was about the same and the contraction for blue was two degrees with a 17/1,000 object.

Complete examination revealed a luetic condition with active paresis and a diagnosis of optic neuritis

on a luetic basis was made.

One gm. of novocain in 500 cc. of saline was given intravenously; three hours after administration, the patient stated that the vision of the left eye had become clearer, although the visual acuity remained the same. Field studies showed an increase in the central field of six degrees with the same test objects.

The following day another gram of novocain was given after which he stated he again could see more clearly. There was again a slight increase in the

size of the central field.

One more gm. was given on the following day. Fields with 5/1,000 white increased to normal size but red and blue did not change. The visual acuity remained at 29/40; 24 hours later another gram

of novocain was given and the patient stated he saw better but no further change of fields or visual

acuity resulted.

Forty-eight hours later the visual acuity increased to 20/30—2 but did not correct further. Fields for white remained full. One more gm. of novocain was administered; 24 hours later the visual acuity was 20/30.

Fundus pictures remained essentially the same except that some of the edema about the disc had subsided. A full field remained. He was then transferred to the neurologic department for treatment of the leutic condition.

#### COMMENT

The diagnosis made was optic neuritis (luetic). There was a noticeable increase in his visual acuity and fields of vision. The beneficial effects were assumed to be due to relief of angiospasm and vasodilatation.

#### CASE 4

A 55-year-old man presented himself for treatment of a perforating injury of the left eye, by a piece of steel. There was a through-and-through perforation near the limbus at the 12-o'clock position and the foreign body was found to be back of the globe upon X-ray examination. No prolapse occurred; the iris was traumatized and the lens injured. The ciliary body was also injured and the patient developed a severe iridocyclitis and cataract formation. The tension rose and was difficult to control.

On indicated treatment the tension dropped to 20 mm. Hg (Schiøtz) and the iridocyclitis subsided. He was discharged from the hospital and returned one month later with a very irritable red eye, secondary glaucoma, and cataract. Severe blepharospasm and lacrimation were present. Atropinization did not relieve the pain, photophobia,

headache, and blepharospasm,

Intravenous administration of one gm. of novocain was started with complete relief of symptoms in about 5 to 7 minutes; 0.25 gr. of morphine did not relieve his symptoms. The intraocular pressure did not drop after the novocain administration. Paracentesis was performed successfully but the tension was difficult to control. The novocain relieved the patient of all symptoms for three days after which time they slowly returned.

Treatments of intravitreal injection of penicillin and intravenous typhoid therapy were given to save the eye. The iridocyclitis and the secondary glau-

coma persisted.

Due to the extreme amount of discomfort, novocain was again given two weeks later. The novocain did not relieve the symptoms but seemed to aggravate them. The cyclitis and glaucoma persisted. The condition went on to enucleation.

#### COMMENT

The diagnosis made was chronic iridocyclitis and secondary glaucoma following perforating trauma. The novocain afforded relief of pain but did not influence the course of the cyclitis nor the course of the associated glaucoma. The glaucoma was judged to be due to the iridocyclitis and to the swelling of the lens. No reduction in intraocular pressure from intravenous novocain could be expected in this instance.

#### CASE

A 39-year-old man complained of almost complete loss of vision of the right eye and was admitted to the hospital for study.

Visual acuity was: R.E., hand movements in the temporal field only; L.E., 20/70, correctible to 20/15. Externally the eyes were normal.

The right disc showed blurred borders and the fundus showed the arteries to be narrowed and the veins distended. No exudates or hemorrhages were present. The fundus of the left eye was normal. He had lost the vision of his right eye over a period of one week. A diagnosis of optic neuritis was made, cause undetermined.

Novocain was started and the usual search for foci of infection was begun. In 24 hours the patient noticed an increase of vision in the peripheral field of the right eye and could count fingers in the temporal and nasal fields. Another gram of novo-

cain was begun.

In view of the seriousness of the condition, intravenous typhoid, penicillin, and vasodilation were begun. Within five days the peripheral field of the right eye enlarged and a central scotoma of five degrees remained. Visual acuity of this eye was now 3/400, corrected. The fundus picture remained unchanged. No foci of infection were found. The patient was discharged and the diagnosis was changed to retrobulbar neuritis, cause undetermined.

### COMMENT

The diagnosis made in this case was retrobulbar neuritis. We felt that no real gain was accomplished from the intravenous novocain. Unless the disease is the result of angiospasm, no beneficial results can be obtained. Not all cases of optic neuritis or retrobulbar neuritis are complicated by factors of vasospasm.

#### CASE 6

A 30-year-old white man was seen with complaints of loss of vision of the left eye. A dimness was noted two days previously and persisted. The right eye had been enucleated for glaucoma six

years previously.

Examination revealed a white left eye with a slight flare in the anterior chamber. Many keratic precipitates were present. The vitreous contained many floating opacities. The fundus appeared normal and the visual acuity was 20/80—2 correctible to 20/30—2. Tensions were normal. A diagnosis of a quiescent type of chronic uveitis was made.

He was admitted to the hospital and a search for foci of infection was begun. One gm. of novocain was given intravenously and, 24 hours later, the patient neticed no change in vision and the flare remained the same. The usual treatments of typhoid, penicillin, and aureomycin were given. No foci of infection were found.

On the third day another gram of novocain was given with no effect. After 30 days' treatment, the flare in the anterior chamber slowly subsided and disappeared. The vitreous cleared slowly but not completely. Visual acuity was 20/25 corrected and the patient was discharged.

#### COMMENT

The diagnosis made was quiescent iridocyclitis. No clinical improvement was noted from intravenous novocain.

#### CASE 7

A 52-year-old white man was admitted to the hospital with a diagnosis of chronic uveitis left eye, secondary glaucoma left eye, and aphakia right eye.

Visual acuity was: R.E., 20/200, corrected, due to endothelial dystrophy which made the cornea cloudy in appearance; L.E., light perception and faulty projection. The left eye showed a ciliary type of injection and gross keratic precipitates were seet; these were white, lardaceous, and very large. The cornea was steamy and the tension was elevated to 39 mm. Hg (Schiøtz).

A complicated cataract was present with heavy posterior synechias. The patient had severe blepharospasm, browache, and pain in the left maxillary

area and the upper teeth.

Intravenous novocain was given for the pain in the usual manner. In 10 minutes the pain completely disappeared, in 20 minutes the blepharospasm was gone and the patient could open his eye. Palpation of the eye also revealed no tenderness. This relief lasted some 16 hours and then the symptoms began to return slowly. Another gram of novocain was administered and the symptoms again disappeared. For the next two days he experienced only an occasional shooting, fleeting pain in the eye.

A search for foci of infection was begun when he was admitted and the uveitis was treated in the usual manner. The secondary glaucoma was controlled with paracentesis. Forty-eight hours after the second administration of novocain, another injection was given. The intravenous typhoid therapy was effective, the eye finally quieted, and the patient was discharged.

### COMMENT

The diagnosis made was chronic uveitis and secondary glaucoma, Intravenous novocain afforded the only relief from pain, No other effects were attributed to this therapy.

CASE 8

A 47-year-old white man was admitted to the hospital\* on August 18, 1949. One week previous to admission he noticed sudden loss of sight in the right eye. There was an altitudinal type of hemianopia which lasted for about one hour and then disappeared. For three days previous to admission he had some blurring, but on the morning of admission he suddenly lost all vision in the right eye.

Past history was negative. Examination of the eyes showed: R.E., central scotoma; unable to count fingers centrally; slight light perception in upper, lower, and temporal fields; pupils equal; reactions to light, both direct and consensual; and tensions were normal. The cornea and iris were normal. The media were clear. Disc was normal. Retinal arteries were small but present. Retinal veins were somewhat dilated. The retina appeared pale, especially in the macular area. A cherry red spot was present. The left eye was normal.

General physical examination was essentially negative except for a systolic murmur in the apical,

aortic, and pulmonary areas.

Laboratory examination showed blood and urine to be normal. X-ray film of the heart was normal. E.K.G. within normal limits.

A diagnosis of occlusion of the central retinal

artery was made.

The patient was given heparin and dicumarol on the chance that the occlusion was embolic in nature. Vasodilators were given and 300 to 500 cc. of 0.1-percent intravenous procaine was given twice daily for two days and then daily for eight days. He was also given papaverine hydrochloride for dilatory effect.

On the second day the vision improved to counting fingers at two and one-half feet. Retinal edema diminished. On the fourth day he could count fingers at 5 to 6 feet. The nasal field was markedly

enlarged.

During the next three days, the fields became nearly full, the central edema of the retina decreased greatly. After this, there was no change and the patient was discharged. There were no pigmentary changes of the retina present on discharge.

#### COMMENT

Diagnosis on this patient was partial occlusion of the central retinal artery.

\* Milwaukee Hospital-Service of Dr. John B. Hitz.

## SUMMARY AND CONCLUSIONS

Intravenous novocain infusions were administered to eight patients in whom the clinical diagnosis suggested the possibility of vasospastic phenomena with and without

the presence of pain.

Cases 2 and 3 showed the best response to the intravenous novocain. In both cases a definite retinal edema was present, Cases 1, 4, and 7 received marked improvement insofar as pain was concerned. There was no effect on vision in Case 5 (retrobulbar neuritis), and a questionable effect in Case 8 (central retinal artery occlusion).

This small series of cases cannot deter-

mine the full value of intravenous novocain in the treatment of ocular diseases. As an analgestic, it appears to have effects and qualities superior to most of the soporifics and narcotics. Its use whenever angiospastic edema is encountered seems to be beneficial and justified.

Further clinical study is warranted, especially in view of the controversial physiologic effects on the acetylcholine-choline-

sterase system,

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# SOME PROBLEMS IN THE DIAGNOSIS AND TREATMENT OF GLAUCOMA\*

THE THIRD MARK J. SCHOENBERG LECTURE

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I deem it a great privilege to participate in this memorial to my old friend, Dr. Mark Schoenberg, whose kindly humanity and abiding enthusiasm made him beloved by all who knew him. Since the problem of glaucoma was so close to his heart, it has seemed to me appropriate to present to you some rather disconnected topics related to that problem.

#### I. TONOMETER STANDARDIZATION

Although the diagnosis of glaucoma does not depend solely on tonometric measurements, there can be no doubt that the reliability of such measurements is of major importance both in the diagnosis of borderline cases and in the evaluation of therapeutic procedures. With the best of techniques and with the best of instruments, there is still an appreciable uncertainty in the reading. Wise ophthalmologists have long been aware of the inevitable margin of error in these measurements. Dr. Schoenberg was among the first in this country to emphasize that, in addition to the necessary minimum errors involved in the clinical application of the tonometer, much larger errors had become widespread as the result of uses of crippled or inaccurately constructed instruments.

In the middle 1930's, with the aid of Dr. Posner, he set up a small testing laboratory in order to examine the physical characteristics of the instruments then in use. These studies<sup>1, 2</sup> revealed that not more than 10 percent of the instruments examined were in good working order and were reliable re-

productions of the original models which they were supposed to represent.

The instrument manufacturers need not be held up for opprobrium on this account, since the ophthalmic profession had given them no guidance as to what specifications they were supposed to meet, and what variations from such specifications were tolerable.

It was chiefly the result of the persistent educational campaign of Dr. Schoenberg that the profession finally became aware of its prime responsibility in this matter. Since the efforts of individuals to remedy this situation were largely ineffective-witness the early work of Schiøtz and of Comberg-it seemed necessary to attack this problem on a national scale and, in 1942, the American Academy of Ophthalmology and Otolaryngology established a Committee on the Standarization of Tonometers which has functioned continuously since that time. Until his death, Dr. Schoenberg was an active member of this committee and contributed importantly to its work.

The work of this committee has been reported from time to time in the *Transactions* of the Academy<sup>8</sup> but, since physicians rarely read technical committee reports and since no recent summary of the work has been published, I should like to report on it to you. I wish to make it clear that this work has been that of the committee as a whole in which I have personally had only a modest share.

As a first step it seemed desirable to set up several tonometer testing stations in addition to that established by Dr. Schoenberg and Dr. Posner, and still operated by Dr. Posner. A station was established in Chicago

<sup>\*</sup> From the Wilmer Ophthalmological Institute of The Johns Hopkins Hospital. Presented before the New York Society for Clinical Ophthalmology, December 5, 1949.

under Dr. Kronfeld, and another in San Francisco by Dr. Harrington and Dr. Shaffer, Over 1,000 tonometers have now been examined by these three stations and the

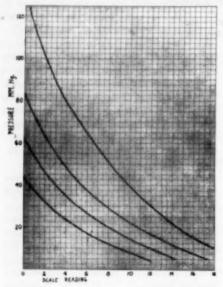


Fig. 1 (Friedenwald), Chart for Schiøtz tonometer approved by the Committee on Standardization of Tonometers (January, 1948).

largest part of these have been reconditioned and recalibrated. I believe that this has constituted a very real service to the profession.

As a basis for recalibration, the committee two years ago adopted a slightly modified Schiøtz scale arrived at as the result of a large set of calibration measurements similar to those originally undertaken by Schiøtz. These calibration measurements were made in my laboratory under a grant from the academy for this purpose. Some of the eyes used in these calibration measurements were supplied by the Eye Bank for Sight Restoration, Inc. The modified Schiøtz scale finally adopted is shown in Figure 1 and Table 1.

The average reading obtained by a properly constructed Schiøtz tonometer on normal eyes of ambulatory patients with this scale is 23 mm. Hg. Similar data for the

Gradle tonometer are shown in Figure 2 and Table 2. Table 3 gives the data required for converting the McLean scale into accord with the Schiøtz and Gradle. One simple way for the practicing ophthalmologist to find out if his tonometer is in proper working order is to measure the tension of about 20 normal adults. If with the new scale the average reading is close to 23 mm. Hg, the instrument can be assumed to be free from serious defect.

In the course of examining and testing many tonometers, the testing stations have discovered more and more mechanical features of the instrument that significantly influence the reading. Gauges and other methods of measurement had to be devised

TABLE 1

Calibration scale for Schiotz tonometers approved by Committee on Standardization of Tonometers (January, 1948)

R	5.5	7.5	10	15
0.00	43.8	61.9	83.2	132.0
0.50	40.5	57.5	77.3	121.9
1.00	37.4	53.3	72.1	113.9
1.50	34.6	49.5	67.4	106.7
2.00	32.0	46.0	62.9	100.2
2.50	29.6	42.9	58.9	94.2
3.00	27.1	40.0	55.1	88.8
3.50	25.4	37.2	51.6	83.8
4.00	23.4	34.7	48.3	79.3
4.50	21.8	32.3	45.3	75.7
5.00	20.1	30.3	42.5	71.8
5.50	18.5	28.3	39.9	68.1
6.00	16.9	26.5	37.5	64.5
6.50	15.6	24.6	35.2	61.0
7.00	14.2	23.0	33.1	57.6
7.50	13.2	21.5	31.0	54.3
8.00	11.9	19.9	29.2	51.1
8.50	11.0	18.5	27.3	47.8
9.00	10.0	17.1	25.6	45.0
9.50	9.0	15.7	23.9	42.3
10.00	8.0	14.4	22.3	39.6
10.50	7.0	13.1	20.9	37.1
11.00	6.2	12.0	19.4	34.6
11.50	5.0	11.1	18.0	32.3
12.00	4.0	10.1	16.7	30.2
14.00		5.7	11.5	21.7
16.00			7.5	15.2
18.00				10.5

in order to measure these features. At present some 20 different physical measurements are regularly made on the tonometers submitted. From time to time clinical comparisons are made with instruments showing different types of aberration and correction

factors are calculated for the various aberrations. I cannot say with assurance that all possible aberrations have been discovered and evaluated, but in the last two years no new aberrations have been encountered.

This analysis of the important common aberrations among tonometers not merely revealed how few subsequently constructed instruments conformed to Schiøtz's original design; they also revealed the fact that there were a great many possible variations not included in the specifications originally drafted by Schiøtz, and that many of these variations significantly affect the clinical reading.

TABLE 2

Calibration scale for Gradle tonometers approved by Committee on Standardization of Tonometers (January, 1948)

			-		
R	0	1	2	3	4
0.00	83.2	96.8	109.9	122.1	133.0
0.50	75.5	87.8	99.5	110.7	122.1
1.00	68.8	80.1	90.6	100.4	109.3
1.50	63.4	73.5	83.1	91.9	99.5
2.00	58.4	67.8	76.6	84.6	91.7
2.50	54.0	62.9	70.9	77.7	84.7
3.00	50.0	58.3	65.8	72.5	78.4
3.50	46.7	54.3		67.5	72.5
4.00	43.6	50.7	57.2	63.0	67.7
4.50	40.8	47.5	53.5	58.9	63.6
5.00	38.2	44.5	50.2	55.2	59.5
5.50	35.9	42.0	47.3	52.0	56.0
6.00	33.8	39.4	44.5	48.9	52.6
6.50	32.0	37.2	42.2	46.1	49.7
7.00	30.4	35.5	40.0	43.8	47.6
7.50	29.0	33.8	37.9	41.6	44.6
8.00	27.8	32.2	36.1	39.5	42.4
8.50	26.4	30.5	34.5	37.6	40.2
9.00	25.3	29.2	32.8	35.8	38.3
9.50	24.2	28.0	31.5	34.3	36.6
10.00	23.1	26.8	30.0	32.7	34.9
10.50	22.0	25.8	28.9	31.5	33.0
11.00	21.1	24.6	27.6	29.9	32.0
11.50	20.3	23.6	26.5	28.8	30.
12.00	19.4	22.6	25.5	27.7	29.3
12.50	18.4	21.8	24.4	26.5	28.
13.00	17.9	20.9	23.4	25.5	27.0
13.50	17.0	19.9	22.2	24.5	26.0
14.00	16.2	19.3	21.7	23.5	24.9
14.50	15.7	18.4	20.8	22.6	24.1
15.00	14.9		19.9	21.8	23.1

As a result of these studies, it has been possible to set up such specifications for the Schiøtz and Gradle tonometers that instruments conforming to these specifications will not give consistently differing readings of more than ±2 mm. Hg on the same eyes.

Since the errors in clinical use are of the order of ±3 mm. Hg, the residual instrumental errors are now of relatively small significance. Arrangements have been made

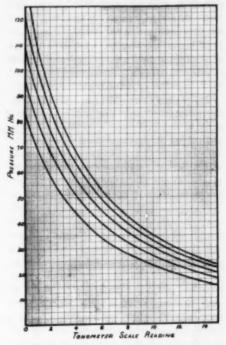


Fig. 2 (Friedenwald). Chart for Gradle tonometer approved by the Committee on Standardization of Tonometers (January, 1948).

with all American manufacturers to conform to these specifications, and instruments that have been certified under the authority of the committee can be assumed to conform to these specifications. The committee cannot be sure that new variants will not occur even within the limits set by these specifications, and any physician who encounters a certified tonometer that seems to be giving aberrant readings should send the instrument to one of the testing stations so that we may have the opportunity to discover the source of the aberration.

Partly as the result of the impetus given by the committee, several manufacturers have made considerable improvements in the design, and instruments of enhanced sensitivity and reliability are now available. An analysis of these improvements in design has been published elsewhere.

# II. OCULAR RIGIDITY

When a tonometer is placed on an eye, the cornea is deformed and indented, and the

TABLE 3

Conversion table—McLean versus Schietz

McLean	Schiøtz	McLean	Schiøtz
10	4.5	36	26.6
11	5.3	37	27.4
12	6.2	38	28.3
13	7.0	39	29.1
14	7.9	40	30.0
15	8.7	41	30.8
16	9.6	42	31.7
17	10.4	43	32.5
18	11.3	44	33.4
19	12.1	45	34.2
20	13.0	46	35.1
21	13.8	47	35.9
22	14.7	48	36.8
23	15.5	49	37.6
24	16.4	50	38.5
25	17.2	55 -	42.7
26	18.1	60	47.0
27	18.9	65	51.2
28	19.8	70	55.5
29	20.6	75	59.7
30	21.5	80	64.0
31	22.3	85	68.2
32	23.2	90	72.5
3.3	24.0	95	76.7
34	24.9	100	81.0
35	25.7		

intraocular pressure is raised above that which was present in the eye before tonometry. What we read with the tonometer is the depth of the indentation produced. What we want to know is the pressure in the eye before the tonometer was rested on it. In order to obtain such information, Schiøtz calibrated his original tonometer on eyes which he obtained at autopsy. He connected the eye with a manometric system, introduced any desired pressure into the eye, and then made a tonometric reading. It is from a long series of such measurements that the Schiøtz chart was obtained by which any given tonometer scale reading with any one

of the four different loads can be read off as some number of millimeters of mercury pressure.

The reliability of applying the Schiøtz chart to a given clinical reading must be held subject to considerable reserve. Suppose we apply the tonometer to two eyes with identical intraocular pressure but differing markedly in the elasticity of their coats. The same amount of corneal distortion and indentation will raise the intraocular pressure higher in the more rigid eye than in the more elastic eye. In spite of the initial equality of the intraocular pressure in these two eyes, the tonometric readings will differ, On the more rigid eye the tonometer scale reading will be smaller, and the intraocular pressure estimated with the Schiøtz chart will be higher than on the more elastic eye. Schiøtz and many of the early workers in the field of tonometry were well aware of this difficulty. They concluded that the tonometer could not determine the true intraocular pressure but only an unspecifiable combination of pressure and rigidity. They were careful, therefore, to describe the procedure as one for measuring "tension" or tonometry, rather than for measuring pressure, that is, manometry. The Schiøtz chart tells us not what was the actual pressure in the eye on which a given tonometric measurement was obtained, but rather what that pressure would have been if that eye had a coat of average of normal rigidity. An important clinical question arises therefore. Are there human eyes whose coats differ so greatly from the average in respect to rigidity that the tonometric measurement may lead to a highly erroneous estimate of intraocular pressure? The answer to this question is that such eyes do exist; though fortunately they are quite rare.8

Twelve years ago, in an attempt to come to grips with this problem, I set out by analyzing previously published work on the distensibility of the eyeball. It turned out that the published data of five previous investigators on eyes from six different mam-

malian species (including man), all fit the simple formula:

(1) 
$$K \frac{dV}{dP} = \frac{1}{P}$$

The value of K varied from eye to eye, but for any given eye was the same at all pressures. It is greater if the eye is rigid than if the eye is readily distensible. It seemed therefore that the numerical value of K could serve as a useful index of ocular rigidity.

If one can assume that the change in pressure for a given change in the volume of the tonometric corneal indentation follows a similar law, then, by knowing the volume of the corneal indentation corresponding to any given tonometric reading, and by taking readings with two different plunger loads, one should be able to calculate the ocular rigidity of the eye measured and correspondingly arrive at a correct estimate of the intraocular pressure. As a first approximation the necessary data could be estimated from Schiøtz's original calibration studies.

The mathematical calculations for any particular pair of readings was, necessarily, quite complex. Reduction of these calculations to some fairly simple graphical operation on a nomogram was successful in making the calculation on the one hand manageable but, on the other hand, considerably more obscure. Very few ophthalmologists have found this graphical computation clinically useful, and I have repeatedly been requested to present the data in tabular form so as to be more easily usable.

Even in the absence of some simple method of reaching an estimate of ocular rigidity and of intraocular pressure corrected for rigidity, there is a very simple way in which the practicing ophthalmologist can tell whether his tonometric estimate with the use of the Schiøtz chart is reasonably accurate or not. If the tonometric readings with two different plunger loads come out to reasonably close agreement, the reading can be accepted as valid and the ocular rigidity

can be assumed to be close to the average normal. If the tonometric reading with the heavier weight is considerably higher than with the lighter weight, then the eye has a high rigidity, and the intraocular pressure is lower than that indicated by either of these readings. If the tonometric reading with the heavier weight is appreciably lower than with the lighter weight, then the eye has a low rigidity and the intraocular pressure is higher than that indicated by either of these readings.

Several years ago the Committee on Standarization of Tonometers felt that the original calibration experiments by Schiøtz should be repeated in the light of modern knowledge and experience. The calibration measurements were made in the laboratory under my direction, and some additional clinical comparisons were made by Dr. Kronfeld. These new data included direct measurements on the volume of the corneal deformation corresponding to various tonometric loads and various intraocular pressures. These new and more reliable data can now be substituted for the indirectly calculated estimates previously used in computing ocular rigidity. More detailed tests showed that the simple equation (1) which expresses the relation between volume and pressure in the case of simple distention of the eyeball needs slight modification before it can be validly applied to tonometric distortion. For the Schiøtz tonometer it was found that a slightly modified equation fitted the data more satisfactorily:

(2) 
$$K \frac{dV}{dP} = \frac{1}{P^{1.85}}$$

For the Gradle tonometer the following equation was required:

(3) 
$$K \frac{dV}{dP} = \frac{1}{P^8}$$

From the experimental data and these two equations, ocular rigidity and pressure can be calculated for any pair of tonometric readings with two different plunger loads.

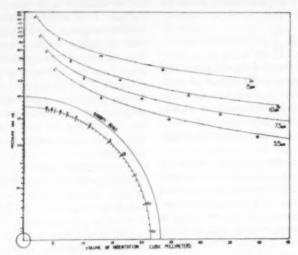


Fig. 3 (Friedenwald). Nomogram for determination of ocular rigidity with Schiøtz tonometer.

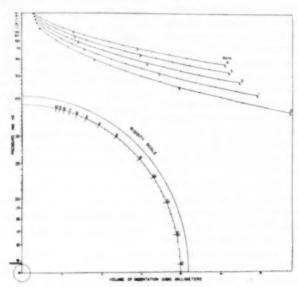


Fig. 4 (Friedenwald). Nomogram for determination of ocular rigidity with Gradle tonometer.

Since in these more complicated equations the absolute value of the rigidity coefficient K loses some of its direct physical significance, it seemed desirable to stress the relative rather than the absolute value of the rigidity. Consequently the computed rigidity coefficients were all multiplied by an arbitrary factor so as to give the average normal rigidity a value of 1.0. On this scale most ocular rigidities fall between values of 0.5 and 2.0. Extreme values under 0.5 and over 2.0 occur in only a few percent of the cases measured, but it is in these few cases that the Schiøtz chart gives significantly erroneous readings. Instances in which failure to take account of this rare phenomenon could lead to erroneous diagnosis have been reported.5

The calculated pressures and rigidities corresponding to various pairs of tonometric readings with two different plunger loads are given in Table 4 for the Schiøtz tonometer, and in Table 5 for the Gradle tonometer. In each box in these tables, the number in the lower left is the pressure in millimeters of mercury, the number in the upper right is the rigidity. Tonometer scale readings are given in steps of one half of a scale unit. Modern tonometers, particularly the electronic tonometer, can be read with reasonable accuracy to one quarter of a scale unit, but a table to include quarter scaleunit readings would be unmanageably cumbersome, for it would require about 40 rows and 60 columns of boxes.

For those who are interested in a higher degree of accuracy than can be given by the one-half scale-unit tables, nomograms have been prepared, Figures 3 and 4. The method of using these nomograms is as follows:

Tonometric readings are taken with two or more different plunger loads, and these readings are recorded as points on the appropriate curves on the chart. A line is then drawn through these points and the intercept of this line on the pressure scale at the left of the chart gives the intraocular pressure. Having drawn this line, a parallel line is now drawn from the center of the little circle in the lower left corner of the chart. The intersection of this line with the rigidity scale gives the reading for rigidity. Copies of these tables and nomograms can be obtained on request from the Committee on Standardization of Tonometers.

## III. FAILURES OF GLAUCOMA OPERATIONS

The literature of recent years has been so heavily loaded with reports on provocative and therapeutic diagnostic tests, and on the medical and psychiatric management of glaucoma cases that these aspects require no special comment at the present time. Some 10 to 20 percent of the operations for glaucoma are unsuccessful in permanently controlling the condition, and it would seem useful to make a fresh inquiry into the causes of surgical failures. A favorable place to begin such an inquiry is the laboratory for eye pathology, for it is in such a laboratory that the eyes with the most conspicuous surgical failures eventually are accumulated. The analysis of the pathologic specimens is, however, not always easy because enucleations are often performed after a long series of operations and accidental contingencies. For this reason a detailed statistical analysis of the causes of failure is not very profitable and I shall, therefore, present only the broad outlines of such a study.

#### SURGICAL OR POSTOPERATIVE ACCIDENT

In about half of the cases, the surgical failure is to be attributed to a surgical accident or to some postoperative accidental contingency. I shall not attempt a complete listing of these accidents since they are familiar to all. This category includes the results of maladroit operations, malplaced incisions, cataract resulting from surgical trauma, operative infections, herniation of the ciliary body, lens, or vitreous into the filtration tract, failure of reformation of the anterior chamber, operative and postoperative hemorrhages, postoperative uveitis, late infection, and so forth. This is the group of

TABLE 4

*.10 gm.	4.0	0 4.5	2.0	3.5	979	6.5	2.0	2.3	8.0	8.5	0.0	8.5	0.01	10.5	0711	11.5	12.0	2.5 13	1.0 11	1.5 14	10.5 11.0 11.5 12.0 12.5 13.0 13.5 14.0 14.5	2 15	15.0 15.5 16.0	5 16.	2 16.1	16.5 17.9 17.5	17.5		18.0 18.5	19.0 19.5 20.0	8.5 M
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Readings With Four Weights

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Readings With Zero Weights

cases in which a fairly obvious explanation exists for the surgical failure.

In the remaining half of the failures, we are confronted with cases in which the operation was technically well performed and was not followed by any dramatic complications. Often the tension is well controlled for an indefinite postoperative interval, but eventually, in these cases, the tension has again gotten out of control. Often repeated surgery has been required in these cases with progressively declining chances of success, progressively increasing risks of contingent accidents. What is the mechanism of failure in these cases?

#### POSTOPERATIVE SCARRING

Microscopic examination of eyes showing failures of this type after the various filtering operations usually reveals that the operative fistula in the corneoscleral tissues is patent, and that good filtration exists out to the episcleral tissues. This finding is in sharp contrast to the frequent closure of the corneoscleral fistula which is to be found in many of the cases where surgical failure is attributable to accidental contingencies, In the absence of such contingencies, the filtration track through the limbal tissues is usually patent but absorption in the episcleral tissues is evidently ineffective. A characteristic feature of these cases is the presence of a dense capsule of fibrous tissue surrounding the episcleral end of the filtration tract. Sometimes there is a large episcleral cavity, the so-called cystoid scar surrounded by a dense fibrous capsule. Sometimes the episcleral end of the filtration tract is closed off by dense adhesions between the conjunctiva and the sclera.

The fact that episcleral and conjunctival scarring play a large role in causing failures in glaucoma surgery is, of course, no news. The clinical experience of the surgeon who has to reoperate these unsuccessful cases has made us all familiar with the tough mattress of scar tissue that we so frequently encounter in attempting to dissect a conjunc-

tival flap in the region of a previous operation. Every limbal operation done under a conjunctival flap leaves some scarring of this type but, in the few cases of successful previous glaucoma surgery in which I have for some reason been forced to re-open the operative region, the degree of scarring has regularly been found to be very much less than in the cases of previous surgical failure.

What are the factors that promote postoperative scarring and what can be done to

reduce the degree of scarring?

- 1. Trauma. Since postoperative scarring results from operative trauma, it is obvious that the operative trauma should be reduced to a minimum. Many surgeons are properly gentle with the intraocular tissues but rather careless in the preparation of the conjunctival flap. Under many circumstances rough treatment of the conjunctiva and episclera does no serious damage, but this is emphatically not the case in regard to the preparation of a filtration bed in glaucoma operations. The general principle of avoidance of undue trauma is one that we can easily give lip service to, but there is very little available knowledge at the present time with which to decide when and under what circumstances is blunt dissection to be perferred to the knife or the scissors.
- 2. Hemorrhage. The absorption of hemorrhage is commonly accompanied by fibroblastic proliferation. It follows that we should leave the filtration bed as dry as possible. Bleeding can sometimes be conveniently stopped with thermal or diathermy coagulation, but these procedures leave some dead tissue which itself promotes scarring, and they should, therefore, be used sparingly. Hemorrhage in the anterior chamber with subsequent seepage into the filtration bed can also contribute a stimulus to the fibrotic process, but the usual absence of fibrin clots in anterior-chamber hemorrhages somewhat mitigates the severity of fibrosis due to hemorrhages in the anterior chamber. It is to be remembered that the framework on which fibroblasts advance into a hemor-

rhage is the fibrin clot. A small anteriorchamber hemorrhage, therefore, usually does little damage to the filtration bed. Large and repeated hemorrhages, on the other hand, can contribute most seriously to the episcleral scarring.

3. Inflammation. It is common experience that filtering operations on glaucoma complicating uveitis have a high percentage of failure. Postoperative as well as preoperative uveitis can in these cases lead to disaster.

4. Previous operations. When the operative bed has already been scarred by a previous operation, the second operation involves much more than the usual amount of trauma, for the fibrous bands resulting from the first operation have to be cut and dissected. The resultant scarring following the second operation is, therefore, usually very much more than that following the first. A filtering operation should, therefore, avoid the site of previous surgery when this is at all possible.

5. Racial and individual factors. It is well known that filtering operations for glaucoma in Negroes show a markedly lower percentage of successes than in whites. A study of eyes enucleated after such failures showed that there was, on the average, more episcleral scarring in the Negro eyes than in those of white patients. Perhaps this is related to the increased tendency toward keloid formation in the Negro, Differences of this type are to be found not only between races but also between individuals of the same race. If the first operated eye of a patient shows a marked tendency toward scarring of the filtration bed, and if this unfavorable course cannot be attributed to one or another of the surgical accidents enumerated above, the chances are pretty high that the second eye, if operated on will follow a similar course. This is by no means an absolute rule, and every ophthalmic surgeon will be able to recall some successes on the second eye after failure on the firstbut the hazards for the second eye are surely

greater when operation on the first eye has failed than when it has succeeded,

6. Postoperative radiation. Operation cannot always be avoided when the risks of failure are high. What can be done to mitigate these risks? Many years ago, in discussing this problem with the late Dr. Curtis Burnham, the question arose as to whether postoperative scarring of the episcleral tissues could be reduced by postoperative radiation therapy. Dr. Coston and I performed a series of iris-inclusion operations on dogs and found that, in this species, the episcleral tissues reacted with very marked fibrous proliferation so that the explanted portion of the iris regularly was surrounded by a dense scar.

This procedure, therefore, seemed a favorable one on which to test the efficacy of postoperative radiation, and a series of animals was studied.

Iris inclusion operations were performed on both eyes of each animal, and only one eye of each was subsequently radiated. On advice of Dr. Burnham, we used the betaray (radon) applicator as a source of radiation, and spread a total dose of 10 gramseconds radiation over an area 2 to 3 times as large as the applicator portal so that each portion of the exposed tissue received 3 to 5 gram-seconds exposure. The application was made one week after the operation and repeated again one week later.

The animals were killed two months after the operation and, on histologic examination, showed appreciably less episcleral scarring in the radiated than in the control eye. No evidence of damage to the intraocular tissues was to be expected following this dosage and none was found.

Following this experiment I have, over a period of many years, applied the same treatment postoperatively to chosen cases of glaucoma. The effective dosage is fairly critical. With half the dose originally suggested by Dr. Burnham, I have found no beneficial effect. With double the dose the filtration bed becomes avascular, and there

is increased danger of fistula formation.

The procedure is not wholly devoid of hazards. At least it has been my impression that there is a higher incidence of late post-operative cataract development in the radiated than in unradiated cases. I would not, therefore, recommend postoperative radiation as a routine procedure in otherwise uncomplicated glaucoma surgery. In those cases that are complicated by severe post-operative hemorrhage, by recent uveitis, by previous surgery, the procedure has, I am sure, very distinct merit.

## POSTOPERATIVE RADIATION IN IRIS ATROPHY

The value of the procedure can be illustrated by histories of two cases of essential without postoperative radiation which resulted in satisfactory control of the tension for about four months. Following this, the tension began to rise again and two cyclodialyses were performed without benefit to the tension. This was followed by a second trephination six months after the first. Like the first trephination, the second was without postoperative radiation. The tension was again controlled for about five months, again returned, and a third trephining operation was performed one year after the first, this time with postoperative beta radiation.

During the succeeding 11 years, there has been no return of the glaucoma, no further loss of vision or of field. The iris atrophy has, however, progressed so that now only

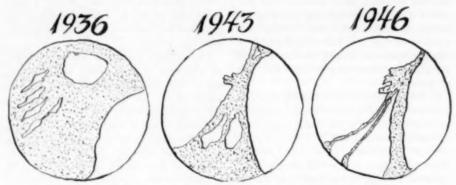


Fig. 5 (Friedenwald). Progressive changes in case of essential atrophy of the iris.

iris atrophy complicated by glaucoma.

The first patient was a woman who consulted me in 1936 when she was 48 years old. She had noticed a "glare" around lights several years previously and had recently had pain and blurred vision in the right eye. Her left eye was normal. Her right eye showed extensive iris atrophy with several holes in the iris. The optic disc was deeply cupped, the visual field was markedly constricted with a Bjerrum scotoma, visual acuity was 20/40 with correction, tension (Schiøtz) was 55 mm. Hg, unaffected by miotics.

A trephining operation was performed

one thin tattered strand of iris tissue runs across the anterior chamber (fig. 5). She was last seen one month ago.

The second patient is also a woman. She came to see me for the first time in June, 1946, when she was aged 37 years. Her right eye had been irritated and sensitive to light for five months previously, and she had first noticed blurred vision in this eye two weeks previously. Her left eye was entirely normal. In the right eye the pupil was horizontally oval and there were several large areas in which the iris stroma was completely absent, exposing the pigment epithelium. Visual acuity and visual fields were

normal, and the disc showed no excavation, but the retinal arteries in this eye showed a collapsing pulsation, and the tension (Schiøtz) was 70 mm. Hg.

Under miotics, the tension was reduced only to 60 mm. Hg, and a trephining operation was performed two weeks after her first visit. Postoperative beta radiation was given.

One month postoperatively she developed a number of retinal hemorrhages in the operated eye. No cause for the hemorrhages was discovered and they disappeared in two weeks. There was a transitory rise of tension (30 mm. Hg) noted on one examination four months after the operation but, aside from this, the tension has not been elevated since the operation. Visual acuity and visual fields have been maintained. No cupping of the optic disc has developed.

This patient has had one additional interesting complication. Fifteen months after the operation she came complaining of lacrimation and discomfort in the operated eye. The tension was very soft and a fluorescein test revealed a fistula in the trephination bleb. The fistula was touched with five-percent silver-nitrate solution and soon healed. There has been no recurrence. In the three years since the operation there has been slight but definite progress of the iris atrophy. The patient was last seen two weeks ago.

Since surgical cures in glaucoma complicating essential atrophy of the iris are extremely rare, the successful control of these two cases following postoperative radiation is worthy of note. The first case is particularly striking since, in this case, four operations were performed without postoperative radiation and without control of the glaucoma. The fifth operation was necessarily performed through a region including scars from previous operations. Postoperative radiation was applied after this fifth operation, and the tension has remained controlled for 11 years in spite of further progress in the iris atrophy.

A statistical report of the cases on which

I have used this procedure would be unilluminating, since I have used this only in cases in which there was reason to expect a high probability of surgical failure. As has already been noted, the procedure is not itself completely devoid of complications. Neither is it a panacea, since failures of control of glaucoma have occurred in the radiated cases. Nevertheless, the proportion of successes has been very much greater than I would have anticipated in these cases had filtering operations been performed without postoperative radiation.

Specifically, I have limited the use of this procedure to cases in which the operative field was scarred by previous surgery, cases in which there had been a recent uveitis, cases in which there was a massive post-operative hemorrhage in the anterior chamber and in the filtration bed, and cases of essential iris atrophy complicated by glauroma.

The procedure has not been successful in my hands in hemorrhagic glaucoma. It is contraindicated in cases of delayed reformation of the anterior chamber since it tends to prolong this delay, but it can be applied in these cases after the chamber has re-formed.

Air injection into anterior chamber as a substitute for paracentesis in emergency control of some forms of secondary glaucoma

In recent years the injection of air into the anterior chamber has been recommended in a number of conditions. The procedure has been found useful in cases of delayed postoperative reestablishment of the anterior chamber, and has been advocated by Chandler<sup>7</sup> as a routine step to be performed at the end of fistulizing operations for glaucoma. In the goniotomy operation, the preliminary replacement of the aqueous by air assists in visualization of the chamber angle and often enables the surgeon to see clearly what he is doing, without the aid and nuisance of a contact glass.

In so far as I am aware, no attention has been paid to the influence of an air bubble in the anterior chamber on the intraocular pressure. In 1937, Dr. Pierce and I published the results of our studies on the intraocular gas exchange. In these experiments bubbles of air or of nitrogen were introduced into the anterior chambers of dogs' eyes, and samples of the gas removed for analysis after varying intervals.

When precautions were taken to avoid gas exchange across the cornea, the steady-state value of the partial pressure of oxygen was found to be 50 mm. Hg; of carbon dioxide, 45 mm. Hg. To these figures must be added the partial pressure of water vapor at 37° C., namely 47 mm. Hg, and four fifths of an atmosphere of nitrogen or 608 mm. Hg, the partial pressure of nitrogen with which, at normal barometric pressures, all body fluids tend to equilibrate.

Adding together these four figures, we obtain the total pressure of 754 mm. Hg which the gas bubble would reach if equilibrium were actually achieved. This is 6.0 mm. below atmospheric pressure, hence the bubble tends to collapse and be absorbed and cannot remain permanently in the anterior chamber. The intraocular pressure was not measured in these experiments. In the surgical manipulation required to remove the bubble, the intraocular pressure appeared to be somewhat below normal, but was surely not negative.

Of the four gas components making up the bubble, it may be assumed that equilibration in respect to water vapor is almost instantaneous. Since the aqueous contains bicarbonate and hence a vehicle for the transport of carbon dioxide, equilibration in respect to this component would also be expected to be very rapid. The experimental results indicate that this is in fact true, and that equilibrizing in respect to carbon dioxide is substantially attained in 15 to 20 minutes.

There is no vehicle for oxygen transport in the aqueous other than the very small solubility of the gas in water but, owing to the oxygen-transporting capacities of the red blood cells, equilibration between the blood and aqueous fluid would tend to be rapid.

The experiments showed that equilibrium in respect to oxygen in the bubble was substantially attained in 2 to 3 hours. After the lapse of such a time interval, the remaining deviations from equilibrium must be essentially limited to nitrogen for which no special transport vehicle is present either in the aqueous or in the blood.

The analysis just given makes it clear that the rate at which the bubble disappears is determined by the excess of the partial pressure of the nitrogen in the bubble over that in the surrounding tissues, and the rate of diffusion of nitrogen through the tissues. In normal eyes this rate is sufficiently slow so that approximately one half of a bubble initially filling the whole anterior chamber is absorbed in 24 hours both in dogs and in

If in the state of slow steady absorption of the bubble something happens to raise the intraocular pressure, then the bubble will be compressed, the partial pressures of all of its components correspondingly raised, and the rate at which it is absorbed enhanced, thus tending to reduce the intraocular pressure toward that of the previous steady state. In this sense the bubble acts as a cushion or safety valve, tending to oppose the effects of factors that raise the intraocular pressure. This is not to imply that, with a bubble in the anterior chamber, the intraocular pressure cannot rise to glaucomatous levels. All that is implied is that, as long as the bubble is present, the pressure cannot go as high as it otherwise would.

The intraocular gas exchange is indeed somewhat more complicated than the outline given above would indicate. In the experiments to which I have referred, we found that rather marked fluctuations in corneal permeability to gases could occur, and that as corneal permeability increased, the partial pressure of oxygen rose and that of carbon dioxide fell, indicating that under these conditions a fairly brisk gaseous exchange occurs across the cornea.

The highest partial pressures of oxygen which we recorded under these circumstances were about 100 mm. Hg, and were associated with carbon-dioxide pressures of 25 mm. Hg. If, to these values, we add the vapor pressure of water, and the atmospheric partial pressure of nitrogen, we reach an equilibrium value of 765 mm. Hg, that is, a pressure of 5.0 mm. Hg above atmospheric. If such a low pressure could be maintained in an eye, the bubble could be expected to persist indefinitely.

In clinical experience in human beings, the bubble is usually completely absorbed in 2 to 4 days, but occasionally persistence of the bubble for longer periods is seen. In such eyes the intraocular pressure must be unusually low and the corneal permeability unusually high.

It is plain from the analysis given so far that the presence of a bubble in the anterior chamber forms a temporary and partial protection against glaucomatous rise of tension, and the question arises as to whether there are any clinical cases in which this effect of an anterior-chamber air injection can be useful. I believe that there are two conditions in which this procedure has some small gifts to offer; namely, in glaucoma complicating active uveitis and in glaucoma complicating hyphemia from blunt injury. In both of these conditions many surgeons reluctantly advocate repeated paracenteses. The reluctance is due to the fact that paracentesis usually reduces the intraocular pressure for only a very short time but, nevertheless, stimulates the formation of peripheral anterior synechias, thus, in the long run, aggravating the glaucomatous process. The advocacy of paracentesis in spite of these deterrants is due to the fact that no more satisfactory procedure for the emergency control of pressure in these cases is available.

Many years ago it occurred to me that withdrawal of aqueous and its replacement by air would, at least, be less productive of peripheral anterior synechias than paracentesis and, in applying this procedure to cases of glaucoma complicating active uveitis, I was surprised to find that the effect in controlling pressure was usually more prolonged than that of a simple paracentesis.

Similar results have followed the application of this procedure to cases of glaucoma complicating hyphemia from blunt injury. In the most severe cases of this type, the blood in the anterior chamber is clotted and cannot be withdrawn through the needle of the injecting syringe. In these cases I have not hesitated to inject a small bubble of air even if no fluid could be withdrawn. This will cause a further rise of pressure for a very short time following which the pressure has, in almost all cases, come down to levels appreciably lower than before injection.

The surgeon who employs this technique must not expect miracles. All that I wish to maintain is that replacement of aqueous by air is preferable to simple paracentesis in those cases in which paracenteses are otherwise reluctantly performed. The argument given above based on the anlysis of the composition of gas bubbles in animals' eyes helps to explain why the procedure may be beneficial.

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# CHANGES IN VISION DURING ADOLESCENCE\*

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The frequency and extent of change in visual acuity, hypermetropia, and heterophoria which occur during adolescence are of interest to those responsible for the eye care of this age group and are questions intimately related to the problem of how frequently the school eye examination should be repeated, Collins and Britten1 tested the visual acuity of 1,072 boys ranging from 13 through 16 years: their results indicate no significant difference in the percentage of boys at each of these ages who had 20/20 vision or who had 20/50 (or worse) vision. These results are to be interpreted in light of the fact that one age group was compared to another age group made up of different boys: the same individuals were not being compared to themselves at different ages.

Ciocco<sup>9</sup> reported the retinoscopic reëxamination of 1,481 school children after an average interval of two and one-half years; only 88 of these were 14 years of age or over at the time of the initial examination. In that age group, myopia developed in 1.3 percent and astigmatism in 11.8 percent within the two and one-half-year period.

This report compares the findings at the initial vision screening examination of 228 boys with the findings on the same boys three years later. All the tests were made at the time of the four annual health examinations and by the same examiner. The modification of the Massachusetts Vision Test was used.<sup>3</sup> At the time of the initial examination the boys' average age was about 14½ years. All the students at a preparatory school who entered that school as first year students in the years 1942, 1943, and 1944, and who remained to enter the fourth year classes three years later, have been included in this survey.

## RESULTS AND COMMENTS

#### VISUAL ACUITY

Table 1 gives the distribution of naked visual acuity for the right eye and for the left eye and shows the percent of the 228 boys whose vision was found to be at each level. These tests were made without glasses whether or not glasses usually were worn. Over this three-year period, no change in the naked visual acuity occurred in the right

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eye in 68.5 percent, and no change in the left eye in 70.5 percent, of the individuals tested.

Those whose visual acuity changed only "one line" on the charts (that is, 20/30 to 20/40, 20/70 to 20/100, 20/100 to 20/200,

change in the visual acuity of the right eye (except the one individual whose vision improved from 20/40 to 20/25) would have been referred to an eye specialist had their vision not already been more thoroughly

TABLE 1
Three-year change in naked visual acuity
(Right eye and left eye)

Change in Visual-Acuity Ratings between Initial Examination	0	.D.	0	.S.
and Examination Three Years Later	Total Number	Percent	Total Number	Percent
No change	156	68.4	161	70.9
20/ 20 to 20/ 25	13	5.7	13	5.7
20/ 20 to 20/ 30	8	3.5	4	1.8
20/ 20 to 20/ 40	3	1.3	8	3.5
20/ 20 to 20/ 50	4	1.8	1	0.4
20/ 20 to 20/ 70	2	0.9	1	0.4
20/ 20 to 20/100	0	0	1	0.4
20/ 20 to 20/200	2	0.9	4	1.8
20/ 25 to 20/ 30	4	1.8	0	0
20/ 25 to 20/ 40	1	0.4	1	0.4
20/ 25 to 20/ 50	0	0	1	0.4
20/ 25 to 20/100	2	0.9	0	0
20/ 30 to 20/ 40	0	0	1	0.4
20/ 30 to 20/ 50	2	0.9	3	1.3
20/ 30 to 20/ 70	- 3	1.3	1	0.4
20/ 30 to 20/200	0	0	2	0.9
20/ 40 to 20/ 50	0	0	1	0.4
20/ 40 to 20/ 70	0	0	1	0.4
20/ 40 to 20/200	1	0.4	0	0
20/ 50 to 20/ 70	1	0.4	2	0.9
20/ 50 to 20/100	1	0.4	0	0
20/ 50 to 20/200	1	0.4	1	0.4
20/ 70 to 20/100	1	0.4	0	0
20/ 70 to 20/200	3	1.3	1	0.4
20/100 to 20/200	0	0	4	1.8
20/100 to 20/200 plus	2	0.9	0	0
20/200 to 20/200 plus	1	0.4	2	0.9
20/ 25 to 20/ 20	2	0.9	4	1.8
20/ 30 to 20/ 20	3	1.3	0	0
20/ 30 to 20/ 25	1	0.4	1	0.4
20/ 40 to 20/ 25	1	0.4	0	0
20/ 50 to 20/ 25	0	0	1	0.4
20/ 50 to 20/ 40	2	0.9	2	0.9
20/ 70 to 20/ 50	2	0.9	1	0.4
20/100 to 20/ 70	2	0.9	0	0
20/100 to 20/100	4	1.8	4	1.8
20/200 plus to 20/200	0	0	1	0.4
Total	228	100.0	228	100.0

20/50 to 20/40, 20/30 to 20/25 and so forth) totaled an additional 44 (15.1 percent) for the right and 40 (15 percent) for the left eye. A change in the right eye of more than "one line" occurred in 16.4 percent, and in the left eye in 14.5 percent.

All of those 40 who showed that much

examined. Only three of the 40 had not previously been corrected with glasses—one whose vision had changed from 20/20 to 20/40, one whose vision had changed from 20/20 to 20/50, and one whose vision had changed from 20/20 to 20/70. Three boys whose vision in the left eye had changed

TABLE 2
THREE-YEAR CHANGE IN NAKED VISUAL ACUITY
(Both eyes)

Change in Visual Acuity Ratings between Initial	0	.U.
Examination and Ex- amination Three Years Later	Total Number	Per Cent
No change	170	74.6
20/20 to 20/25	9	4.0
20/20 to 20/30	7	3.1
20/20 to 20/40	5	2.2
20/20 to 20/50	1	0.4
20/20 to 20/70	1	0.4
20/20 to 20/100	2	0.9
20/20 to 20/200	1	0.4
20/30 to 20/40	2	0.9
20/30 to 20/50	2 1 2 1	0.4
20/40 to 20/50	2	0.9
20/40 to 20/70	1	0.4
20/50 to 20/70	4 1 1 2 2 2	1.8
20/50 to 20/100	1	0.4
20/50 to 20/200	1	0.4
20/70 to 20/100	2	0.9
20/70 to 20/200	2	0.9
20/100 to 20/200	2	0.9
20/100 to 20/200 plus	1	0.4
20/25 to 20/20	4	1.8
20/50 to 20/25	1	0.4
20/50 to 20/40	2	0.9
20/200 to 20/70	3	1.3
20/200 to 20/100	3	1.3
Total	228	100.0

from 20/20 to 20/40 and one whose change was from 20/20 to 20/200 had not previously had glasses.

Naked visual acuity for both eyes is

shown in Table 2. There was no change over this three-year period in the visual acuity with both eyes in 170 out of the 228 boys (74.5 percent). In this same period nine (3.9 percent) showed a slight and four others (1.7 percent) showed a more marked improvement in visual acuity. There was a decrease of vision of "one line" in 28 (12.3 percent) and of more than "one line" in 17 (7.5 percent.)

In this latter group of 17 there were only two (both had changed from 20/20 to 20/40) who had not been given glasses by the time of the final examination. In this connection it is well to point out that this survey was made on a group of relatively high economic status and also one which has the benefit of a thorough annual health examination.

Table 3 shows the year change in visual acuity revealed by the annual eye examination of a few subjects: only one of them (N. N.) had had any illness of any consequence during the three-year period. He had measles during the year prior to his third examination. The number in this group who showed a significant change in naked visual acuity would alone seem to justify, and to suggest the desirability of, an annual visual screening examination of adolescents.

TABLE 3
CHANGE IN NAKED VISUAL ACUITY DURING A THREE-YEAR PERIOD SHOWN BY FOUR SUCCESSIVE ANNUAL EYE EXAMINATIONS

Name		H. H.			W. L.			N.N.	
Eye	O.D.	O.S.	O.U.	O.D.	O.S.	O.U.	O.D.	O.S.	O.U.
Naked Visual Acuity									
1st examination	20/ 20	20/ 20	20/ 20	20/20	20/ 20	20/ 20	20/ 20	20/ 30	20/ 204
2nd examination	20/ 25	20/ 20	20/ 20	20/ 20	20/ 20	20/ 20	20/ 25	20/ 50	20/ 20*
3rd examination	20/200	20/100	20/ 50*	20/ 20	20/ 20	20/ 20	20/ 70	20/ 70	20/ 704
4th examination	20/200	20/200	20/100*	20/50	20/200	20/40	20/200	20/200	20/200
Name		F. P.			Н. Т.			L. L.	
Eye	O.D.	O.S.	O.U.	O.D.	O.S.	O.U.	O.D.	0.5.	O.U.
Naked Visual Acuity									
1st examination	20 / 25	20/30	20/ 20	20/20	20/ 20	20 / 20	20 / 25	20/20	20 / 20
2nd examination	20 / 40	20/ 70	20/ 25*	20 / 70	20/40	20/ 30	20 / 20	20/ 20	20/ 20
3rd examination	20 / 70	20/100	20/ 70*	20/200	20/200	20/200*	20/100	20/100	20 / 50
4th examination	20/100	20/200	20 / 70*	20 / 70	20/100	20/ 50*	20/100	20/200	20/1005

<sup>\*</sup> Had been given glasses prior to this examination,

TABLE 4
Change in performance on the plus 1.5D test of hypermetropia over a period of three years

Both Eyes	Number who did not have Glasses at Either the Examination or Three Years Later	Number who had Glasses at One Examination but not at the Other	Number who had Glasses at Both Examina- tions	Total Number
No change	120	33	67	220
From fail to pass	5	0	0	5
From pass to fail	3	0	0	3
Total	128	33	67	228

# HYPERMETROPIA

The presence of a significant degree of hypermetropia was determined on the basis of the subject's ability to read the 20/20 line through plus 1.5D. sph.<sup>a</sup> The plus 1.5D. sph. were placed over the subject's own glasses if he had glasses and therefore these data are of little value. There was no change in the test results of the 110 boys who wore glasses at either the initial test or the final test or at both of these times (table 4).

Five of the 120 boys who did not wear glasses at the time of either of these examinations passed at the second test although they had failed it three years earlier, possibly indicating a lessening of hypermetropia. Three of the same group changed their rating from pass to fail within that same period.

The fact that this test was administered with the subject wearing his own glasses makes it impossible to tell what change may have occurred in the 33 who wore glasses at one examination but not at the other and therefore also makes it impossible to determine what percent of the entire group of 228 developed hypermetropia during the three-year period. It can only be said that the ability to pass this plus 1.5D, sph. test changed during the three years in eight of the 120 boys who did not wear glasses at either examination time.

#### HETEROPHORIA

Heterophoria at 20 feet was determined by the subject's response to a Maddox cross

viewed through spectacles in one pair of which a red multiple Maddox rod was mounted horizontally for the right eye and in the other pair a red multiple Maddox rod was mounted vertically for the right eye; there was no lens before the left eye.1 Heterophoria at near was determined by the subject's response to a test card held at 16 inches and viewed through a 3.0 D. prism mounted base-up before the right eye and base-down before the left eye.3 If the subject had glasses, they were worn for these tests. A referral or "fail" rating was given when more than four prism diopters of exophoria. six prism diopters of esophoria, one prism diopter of hyperphoria for distance, or six prism diopters of esophoria, or eight prism

TABLE 5
CHANGES IN HETEROPHORIA OVER A PERIOD OF THREE YEARS

	Horizontal (distant)	Vertical (distant)	Horizontal (near)
	Total Number	Total Number	Total Number
Change in Prism Diopters	-		
No change	115	210	113
1	72	12	70
2 3 4 5 6 7	25	3	26
3	7	0	7
4	3	1	6
5	1	-	0
6	2	-	1
7	0	-	1
8	0	-	1
Unable to do	1	1	2
Not recorded	2	1	1
Total	228	228	228

diopters of exophoria for near was found.

The number of subjects who had the same rating at each of the examinations is extraordinarily high in view of the great variability of results, which is a common feature of these tests. When those who changed only from one to four diopters are added to those for whom no change was recorded, the percentage of those in whom only an insignificant change was noted is raised in each instance to over 97 percent (table 5). During this period only two of the 228 boys changed from a pass to a fail rating on this test. One subject increased from five to nine prism diopters esophoria (distant); another from one to seven prism diopters esophoria (near). The four subjects whose hyperphoria changed more than one prism diopter failed the test at both the initial and final examination

## SUMMARY

1. The frequency and extent of changes in naked visual acuity, hypermetropia, and heterophoria which occurred in a group of 228 adolescents who were examined annually

over a three-year period using a modification of the Massachusetts Vision Test are reported and discussed.

2. No change in the naked visual acuity of both eyes was noted in 74.5 percent of the group during the three-year period. There was a decrease of more than "one

line" in 7.5 percent.

3. Tests for hypermetropia were made with the subject wearing glasses if he had been given them, so the data concerning this part of the screening examinations are of little value.

- 4. There was little change in the results of the tests for heterophoria over this threeyear period: only two of the group showed sufficient modification in heterophoria to change them from a "pass" to "fail" rating in this interval.
- 5. Although the frequency and extent of the changes in visual acuity observed in this group are not great, they are sufficient to suggest the desirability of an annual visual screening examination of adolescents.

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## OPHTHALMIC MINIATURE

Humboldt tells, in his Cosmos, of a tailor in Breslau named Schön, who also had seen the satellites of Jupiter with the naked eye. No examples of a greater range of vision are known.

> Wonders of the Human Body, A. le Pileur, 1870.

# THE EFFECTS OF PROCAINE AND COCAINE WHEN APPLIED LOCALLY TO THE IRIS\*

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### I. INTRODUCTION

Retrobulbar injections of procaine hydrochloride had been shown by us¹ to produce the effect of a temporary ciliary ganglionectomy by blocking the ciliary ganglion and the postganglionic ciliary nerves. The pupil on the injected side dilated promptly. This dilatation was easily overcome by pilocarpine instilled into the conjunctival cul-de-sac, but physostigmine was ineffective until the procaine had begun to wear off, often for as long as two hours. Pilocarpine, therefore, had been suggested as the miotic agent of choice when a miosis was desirable in the presence of retrobulbar anesthesia.

During the course of this earlier work, certain observations were made which suggested that procaine had a rather strong mydriatic action when applied locally to the iris but that the mechanism was quite different from the mydriasis resulting from retrobulbar injection. These observations led to the work to be reported in this paper which is devoted solely to the studies upon the effect of procaine when applied directly to the iris.

#### II. OUTLINE OF EXPERIMENTS

This work is divided into two parts:

#### PART I

Observations of disturbances of pupillary motility resulting from local application of

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procaine hydrochloride to the iris through three different routes: (A) Injection into the anterior chamber; (B) instillation into the conjunctival cul-de-sac; (C) subconjunctival injection.

#### PART II.

Studies to determine the mechanism by which procaine applied directly affected the iris.

# III. METHOD OF EXPERIMENTS

Unless otherwise stated, all experiments were carried out on dogs anesthetized with nembutal given intravenously. The term retrobulbar injection refers throughout to the injection of two cc, of four-percent procaine hydrochloride. This was accomplished by rotating the eye upward with the fixation forceps and inserting the needle through the lower eyelid. If a retrobulbar injection was to be repeated, the syringe was detached and the needle left in place between injections.

Whenever a drug was to be injected directly into the anterior chamber, a sharp 27-gauge needle was inserted through a beveled corneal route starting at the limbus. Aqueous was aspirated and replaced by an equal amount of the solution containing the drug. When drugs were used in the conjunctival cul-de-sac, two instillations were made, at five-minute intervals, in order to insure absorption.

All pupillary measurements were estimated by use of a millimeter ruler. Figures given represent the averages of the eyes tested. Pupils were arbitrarily said to be miotic when three mm. or less in diameter. In clinical experiments on man, measurements were performed in exactly the same manner.



Fig. 1A (Scheie and Ojers). Before procaine injection following nembutal anesthesia.

#### IV. OBSERVATIONS

# PART I

Observations of disturbances of pupillary motility resulting from local application of procaine hydrochloride to the iris

A. Effect of procaine hydrochloride injected into the anterior chamber

1. Disturbance in pupillary motility. Twotenths cc. of aqueous was aspirated and replaced by 0.2 cc. of four-percent procaine in the anterior chamber of the eyes of several different species and its effect upon the pupil was noted (table 1). In 37 dog eyes prompt wide pupillary dilatation resulted, the pupils changing from a size of 1 to 2 mm. to an average of 8 to 10 mm. in diameter in a matter of seconds (fig. 1, A and B). These pupils remained larger than three mm. for four and one-half hours. The pupil of the

TABLE 1

Pupillary dilatation resulting from procaine injected into anterior chamber

(0.2 cc. aqueous aspirated and replaced by 0.2 cc. 4% procaine HCl)

Species	Number of Eyes	Pupillary Size before Injection	Pupillary Size after Injection
Dog	37	1-2 mm.	8-10 mm.
Cat	1 5	3-4 mm.	9 mm.
Rabbit	1.3	4-5 mm.	5- 6 mm.

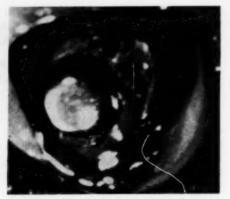


Fig. 1B (Scheie and Ojers). Mydriasis produced by an intrachamber injection of 0.2 cc. procaine hydrochloride (four percent) into the eye of a dog anesthetized with intravenous nembutal (fig. 1A). Aqueous humor (0.2 cc.) withdrawn just prior to procaine injection.

eye of the cat behaved likewise, but dilatation was much less in the eye of the rabbit.

2. Altered response to pilocarpine and physostigmine. These dilated pupils were then tested with pilocarpine and physostigmine and were found to react in a quite different manner from those dilated by the retrobulbar injection of procaine. Not only physostigmine but also pilocarpine failed to produce miosis (table 2).

In dogs, one-percent pilocarpine required two hours to produce a miosis in eyes with the pupils dilated by procaine injected into the anterior chamber as compared to 24 minutes in those dilated by the retrobulbar injection of procaine.

In cats, pilocarpine constricted pupils which had been dilated by retrobulbar injection of procaine to the size of three mm. in 15 minutes, whereas, when dilated by procaine in the anterior chamber, a diameter of seven mm. or more persisted for two hours and longer. Physostigmine was equally ineffective used alone or in combination with mecholyl.

The combination of one-half percent physostigmine and 20-percent mecholyl used in eight dog eyes required 90 minutes to pro-



Fig. 2 (Scheie and Ojers). Mydriasis produced in human eye following instillation of 10-percent procaine hydrochloride in 1:3,000 zephiran into left cul-de-sac.

duce a miosis of three mm. when the pupils had been dilated by procaine in the anterior chamber but constricted pupils dilated by the retrobulbar injection of procaine in 10 to 15 minutes.

B. Effect of procaine hydrochloride instilled into the conjunctival cul-de-sac

Procaine was found to have no mydriatic effect when ordinary aqueous solutions were instilled locally into the eye. However, when its absorption through the cornea is increased by wetting agents, mydriasis does result. Twenty-seven human subjects were tested by using 10-percent procaine in a solution of 1/3,000 phemerol, two drops, five minutes apart. Mydriasis, averaging 2.2 mm., was produced in 21 minutes (fig. 2). This persisted for two hours. Three or four drops would produce a small but measurable impairment of accommodation, probably due to depression of parasympathetic nerve supply or to a direct effect upon the ciliary muscle itself.

# C. Procaine injected subconjunctivally

One cc. of four-percent procaine was injected subconjunctivally in dog eyes but no change in pupillary size resulted. We at-

tempted to simulate cataract extraction by injecting procaine beneath the flap, turning down the conjunctival flap and opening the eye, but our findings were of little value in view of the fibrinous exudate which accumulated in the pupillary space to prevent accurate evaluation of results.

This same experiment was repeated in heparinized dogs. Five of the nine dog eyes used became markedly miotic upon turning down the corneal section. The irises of the remaining four eyes remained semidilated and failed to constrict to pilocarpine dropped directly onto the wound. The experiments with the heparinized animals were complicated by the accumulation of uncoagulated blood from the wound edges which accumulated in the anterior chamber.

Information was obtained from 10 dog eyes, however, in which pupils were first dilated with the retrobulbar injection of procaine. Following subconjunctival injection of procaine, a conjunctival flap was dissected downward to the limbus but the anterior chamber was not entered. Pilocarpine instilled in these eyes produced miosis after an average of 60 minutes which is in contrast to 24 minutes in eyes which had received only a retrobulbar injection (table 3). In

TABLE 2
Antagonistic effect of procaine to miotic drugs
(0.2 cc. aqueous aspirated and replaced by 0.2 cc. 4% procaine HCl)

Miotic	Species	Normal	Procainized
Pilocarpine 1% Pilocarpine 1% Physostigmine 0.5% and	Dog eyes (10) Cat eyes (5)	3 mm. in 24 min. 3 mm. in 15 min.	3 mm. in 2 hours 7 mm. in 2 hours
Mecholyl 20%	Dog eyes (8)	3 mm. in 15 min.	3 mm. in 90 min.

man, the subconjunctival injection of procaine produced only a slight anisocoria.

#### Conclusions

These experiments showed that procaine, when applied directly to the iris, produced a rather marked and profound mydriasis. The fact that both pilocarpine and physostigmine were rendered inactive suggested that the disturbance was either at the motor end-plate simulating the action of atropine, or due to a depression of the muscle cell itself, peripheral to the motor end-plate. It might also have been considered possible that the dilator

similar to those of cocaine. These two substances, in fact, share several other physiologic properties.

Four of these are pertinent to our present discussion because each is capable of producing mydriasis: (A) Local anesthetic effect; (B) sympathomimetic properties; (C) central stimulation of central nervous system; (D) depressant action upon muscle cells.

A. Local anesthetic effect upon individual nerve fibers which blocked the ciliary ganglion and the postganglionic ciliary nerves: We observed pupillary dilatation re-

TABLE 3

EFFECT OF SUBCONJUNCTIVAL PROCAINE UPON (1) PUPILLARY SIZE AND (2) RESPONSE TO PILOCARPINE

Species	Number of Eyes	Conjunctival Flap Dissected	Effect
Dog	6	0	No change in size
Cat	2	0	Irregular pupil
Dog	10	+	3 mm. in 60 minutes following pilocarpine
Dog	2	Chamber opened	Miosis greatly delayed

muscle had been strongly excited.

Because cocaine, also a local anesthetic, has long been known to be an effective mydriatic agent when dropped into the conjunctival cul-de-sac, a comparison with procaine seemed in order. We therefore carried out all of the aforementioned experiments with cocaine, although in a smaller number of animals, and found nearly identical results.

#### PART II

Site of action of procaine and cocaine in pupilloconstrictor mechanism when applied locally

Cocaine is ordinarily thought to produce mydriasis through a sympathor imetic action when dropped into the conjunctival cul-desacs as shown by Limbourg 1892, and Schultz, 1898. This substance has greatly interested physiologists and phyrmacologists for years and it has been the subject of many investigations. Procaine likewase has been shown to have sympathomize for properties

peatedly following the use of procaine in retrobulbar injections which blocked the ciliary ganglion. These pupils, however, constricted promptly with pilocarpine in contrast to those dilated by procaine applied directly to the iris.

# B. Sympathomimetic action:

Limbourg,<sup>2</sup> in 1892 and Sihultz,<sup>3</sup> in 1898, showed that cocaine instilled in the conjunctival cul-de-sacs dilated normal pupils but caused no change following the removal of the superior cervical ganglion. Because of these and other observations, cocaine has been said to be a sympathomimetic drug. Considerable work has been done particularly on cocaine since that time, demonstrating that it does have a sympathomimetic action. It is known to augment the action of adrenalin when given systematically, a property which procaine also has.

Philpot,4 in 1940, demonstrated that cocaine, procaine, and certain other anesthetics inhibited the amine oxidase (one of the physiologic substances which destroys adrenalin) of rat and guinea pig liver, as well as certain other oxidases. This evidence indicates that procaine, as well as cocaine, has a sympathomimetic action comparable to the parasympathomimetic effect of physostigmine which also protects the effector substances.

If this were true, cocaine and procaine should produce no mydriasis when injected into the anterior chamber following removal of the sympathetic nerve supply to the eye. brane on the operated side. On the 4th, 18th, and 28th days following sympathectomy, procaine injected into the anterior chamber of these animals produced prompt maximal mydriasis (table 4).

## Conclusions

We concluded from this information that a profound mydriasis resulting from the anterior-chamber injection of cocaine and procaine had not resulted from their sympathomimetic action. The fact that some

TABLE 4

Effect of intrachamber calcium gluconate and four-percent procaine on eyes of dogs
with cervical postganglionectomy
(Pupil Size in Millimeters)

Eye	Number of Days after Ganglionectomy	Before Block	After Retrobulbar Block	Following 0.2 cc, Intrachamber Calcium Gluconate 10%	Folks	owing 6	0.2 cc. l nine Hy	ntrach	ambe oride
						1	minute	8	
					5	10	15	20	25
1	4	2	district.	NAME OF TAXABLE PARTY.	8	8	8	9	9
2	4	2	- 8		6	8			
. 3	11	2	10	i	5	7	7	8	
4	11	2	12	1	5	6	7	7	
5	14	2	8	2	6	9	9		
6	18	2			8	8	5	5	
7	18	1	-	Pro00	9	9	9	9	
8	21	2	8	2	6	7	8	8	
0	28	1		-	6	7	8	8	

The following experiments were therefore undertaken,

# Experiments

a. Animals were injected with dibenamine hydrochloride, a substance which is said to be adrenalytic and at least partially sympatholytic.<sup>8</sup> Dogs were given 30 mg. of dibenamine hydrochloride per Kg. of body weight intravenously. Procaine or cocaine injected into the anterior chamber of these animals produced the same amount of mydriasis as had occurred in normal controls.

b. Postganglionic cervical sympathectomies were performed on three dogs. Twenty-four hours later all of the animals exhibited narrowed palpebral fissures, miotic pupils, and a nonretracted nictitating memdegree of cycloplegia results from the local instillation of procaine in human subjects also suggests some interference with the parasympathetic innervation or with the ciliary muscle directly, also serving as evidence against the sympathomimetic action of these drugs. Finally, pupils dilated by procaine or cocaine applied locally became 1 to 2 mm. larger following the application of neosynephrin or adrenalin suggesting that at any rate maximal sympathetic stimulation had not occurred. This seemed unlikely considering the profound nature of the mydriasis produced by procaine and cocaine.

C. Central stimulation when given intravenously:

MacGregor,6 in 1939, compared the effects

of cocaine and procaine upon various structures in the body including observations upon pupil size. He found that the intravenous injection of either escaine or procaine caused dilatation of nurmal and denervated pupils. He corrobe ated previous observations by Schultz<sup>3</sup> that cocaine instilled locally, however, dilated only the normal pupil and had no effect on the denervated pupil. Procaine locally dilated neither type of pupil.

In concluding his paper, this author posed the problem: Why was it that the denervated that the intravenous injection of cocaine caused pupillary dilatation on that basis.

# D. The curarelike action on muscle cells:

Harvey<sup>7</sup> and MacGregor,<sup>8</sup> studying the effect of procaine and cocaine on the mammalian skeletal muscle and on neuromuscular transmission, found that each had curarelike action. Harvey stated that neuromuscular transmission was blocked probably at the motor end-plate, leaving the response of the muscle to direct stimulation unimpaired. MacGregor, however, found that, in addition

TABLE 5
EFFECTIVENESS OF MIOTIC ASENTS WHICH STIMULATE WITH DIRECT EFFECT UPON MUSCLE CELL

Species Eye		Miotic	Amount	Pupillary Size Before After (mm.)	Time
Dog Rabbits	1 2 3 4 5 10 eyes	Histamine Histamine Histamine Histamine Histamine Histamine	0.3 mg. 0.3 mg. 0.3 mg. 0.3 mg. 0.3 mg. 0.3 mg.	8 4.5 10 3.5 10 10.0 10 10.0 11 5.0 5 5.0	20 min 10 min 60 min 60 min 50 min 60 min
Dogs	1 2	Barium chloride Barium chloride	0.2 cc. 1% 0.2 cc. 1%	8 5.0 9 7.0	25 min 20 min
Dogs	1 2 3 4 5 6 7 8	Calcium gluconate	0.1 cc. 10% 0.1 cc. 10%	10 1.0 9 1.0 9 1.0 10 1.0 10 1.0 8 1.0 10 1.5 9 1.0 10 1.0	10 min 10 min 10 min 10 min 10 min 10 min 10 min 10 min 10 min

pupil reacted as well as the normal pupil to the intravenous cocaine, but was insensitive to the external application of cocaine, and why, on the other hand, did procaine which had no mydriatic action when applied externally, dilate both the normal and the denervated pupil when given intravenously? The author offered differences in absorption of drugs as a possible explanation.

In reviewing MacGregor's work, it is seen that the animals upon which he was working were not decerebrate. He probably observed pupillary dilatation due to the central action of cocaine, for it has been known for years to the curarelike action on skeletal muscle, the contractility or excitability of the muscle cells themselves was depressed and that this action was peripheral to the motor end-plate and upon the motor cell itself.

No mention was made of its effect upon smooth muscle nor is there any mention in the literature of the possible effect upon the peripheral parasympathetic mechanism, but it did seem that this mechanism could easily explain the effects of procaine and cocaine following local application to the iris. The method of proof seemed to rest with use of substances capable of stimulating muscle cells directly. Those easily available were calcium, barium, and histamine which we tested on several normal pupils (table 5). Calcium proved to be the most effective miotic agent of these substances. Even though histamine had been claimed to be the most effective miotic agent we found its effect unpredictable,

# Experiments

a. Effect of calcium upon pupils dilated by procaine and cocaine. Pupils were first di-



Fig. 3A (Scheie and Ojers). Pupil of nembulatized dog dilated with intrachamber injection of 0.2 cc. procaine hydrochloride (four percent).

lated by injecting 0.1 cc. of procaine or cocaine (four percent) into the anterior chamber (fig. 3A). The same amount of calcium gluconate was then injected in a similar way (fig. 3B), Very little pupillary contraction had occurred at the end of an hour (table 6, part I).

b. Effect of procaine and cocaine upon pupils constricted by calcium ions. Miosis was obtained in two eyes by injecting calcium gluconate and the effect of subsequent injection of procaine was observed. Fairly prompt pupillary dilatation resulted (table 6, part II). These experiments seemed to point quite definitely to a local depressant action upon the muscle cell itself. Calcium gluconate was unable to overcome procaine mydriasis. On the other hand, miosis due to calcium gluconate was easily counteracted by procaine.

Mydriais was produced in a few dogs by atropine and homatropine which theoretically block the motor end-plate. Calcium then injected into the anterior chamber produced prompt miosis (table 7).

## Conclusions

The fact that procaine dilates pupils contracted by calcium, a substance which stimu-

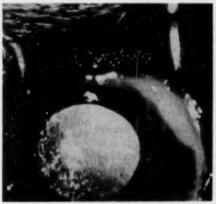


Fig. 3B (Scheie and Ojers). Antagonism of procaine to calcium-gluconate mioris. Same eye as in Figure 3A after intrach. mber injection of 0.2 cc. calcium gluconate (10 percent).

lates the muscle cell directly, strongly suggests that procaine causes pupillary dilatation through depression of the sphincter muscle cells themselves. This is further suggested by the fact that calcium is unable to constrict pupils dilated beforehand by procaine; whereas, when atropine or homatropine are used, miosis results rather promptly.

#### V. DISCUSSION

Procaine applied directly to the iris produces a mydriasis entirely unrelated to its effect by retrobulbar injection. A procainized iris is not only resistant to physostigmine but

#### TABLE 6

#### ANTAGONISTIC EFFECT OF PROCAINE HCI AGAINST CALCIUM GLUCONATE

 Pupils of dog eyes dilated by 0.1 cc. procaine HCl (4%) in anterior chamber followed by immediate injection of 0.1 cc. calcium gluconate (10%).

Eye	Size after Procaine	Size 60 minutes after Calcium Gluconate
1	9 mm.	9 mm.
2	8 mm.	5 mm.
3	8 mm.	5 mm.
4	10 mm.	7 mm.
5	10 mm.	9 mm.
6	9 mm.	7 mm.
7	10 mm.	7 mm.
8	9 mm.	8 mm.

II. Pupils of dog eyes constricted by calcium gluconate in anterior chamber followed by immediate injection of 0.1 cc. procaine HCI (4%).

Eye	Size after Calcium Gluconate	Size 10 minutes after Procaine HCI	
1 2	1.5 mm. 1.0 mm.	8 mm. 8 mm.	

is unaffected by pilocarpine or calcium. This effect does not appear to be due to a central stimulation by procaine for several reasons. In the first place, intravenous procaine gives a very short-lived mydriasis, while that due to procaine injected into the anterior chamber lasts two hours or longer. The degree of mydriasis and the fact that miotics are rendered ineffective also speaks against a central origin.

Mydriasis due to the sympathomimetic action of procaine also seemed unlikely. As has been mentioned when pupillary dilatation had been obtained by procaine and cocaine, further dilatation, to the extent of 1 to 2 mm., was observed after the instillation of neosynephrin or adrenalin which stimulate the dilator muscle. Procaine mydriasis occurred in the presence of blocking of the sympathetic system with large doses of dibenamine and after sectioning of the postganglionic sympathetic fibers; and finally, the partial cycloplegic action observed in humans should result from interference with

the ciliary muscle or its parasympathetic innervation.

The concept that procaine produces a direct effect upon the sphincter mechanism is supported by many of our results. The ineffectiveness of pilocarpine and physostigmine in overcoming procaine mydriasis indicated that procaine had either blocked the motor end-plate, as does atropine, or that it had depressed the muscle cell directly.

Experiments showed that procaine applied locally to the iris could prevent miosis by calcium ions or would promptly dilate pupils already constricted by these ions which

#### TABLE 7

THE EFFECT OF CALCIUM GLUCONATE UPON PUPILS DILATED BY HOMATROPINE

(2% homatropine HBr 0.2 cc. into anterior chamber followed by 0.2 cc. 10% calcium gluconate)

	Size after	Size after Calcium Gluconate			
Eye	Homatropine mm.	15 minutes mm.	25 minutes mm.		
1	9	3	2		
2	10	4	3		
3	10	3	2		
4	11	5	4		
5	8	.5	2		

stimulate the muscle cells directly. From those observations, we must conclude that all evidence suggests that procaine depresses the cells of the sphincter muscle of the iris preventing response even to direct stimulation of that structure.

#### VI. CONCLUSIONS

- Procaine hydrochloride when injected into the anterior chamber produced a mydriasis in dogs and cats which persisted for several hours.
- Pilocarpine and physostigmine are both incapable of overcoming mydriasis produced by the anterior-chamber injection of procaine.
- Mydriasis produced by procaine applied locally to the iris probably resulted from depression of the cells of the sphincter muscle itself: (a) Sympathomimetic action

appeared unlikely because the same mydriasis occurred in animals from which the cervical sympathetic nerves had been removed postganglionically. (b) Calcium ions, which stimulate muscle cells directly, were incapable of overcoming the mydriasis.

4. The instillation of 10-percent procaine in solution with 1/3,000 phemerol produced mydriasis in human subjects. Some disturb-

ance of accommodation could be noted occasionally.

5. Clinically, when prompt mioses is desirable following surgery, the use of procaine beneath the subconjunctival flap should be avoided. When the chamber is open procaine can contaminate the iris preventing subsequent pupillary constriction.

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# THE EFFECT OF CERTAIN HYDROGENATED ALKALOIDS OF ERGOT ON GLAUCOMA\*

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This is a preliminary report on the results obtained in chronic and acute glaucoma with the use of a group of hydrogenated ergot alkaloids† which have recently become available for clinical trial. These agents, dihydroergocornine (DHO 180), dihydroergocristine (DCS 90), and dihydroergokryptine (DHK 135) were first isolated and chemically defined in 1943 by Stoll and Hofmann.¹ Pharmacologic analyses by Rothlin,²

Orth,<sup>8</sup> Bircher and Cerletti,<sup>4</sup> and others indicated that these compounds possess therapeutic properties of major interest. A rapidly growing literature has confirmed the clinical value of these drugs in hypertension and certain types of peripheral vascular disease.<sup>5-9</sup>

The pharmacodynamic action of the hydrogenated ergot alkaloids is characterized by a complicated interplay of central and peripheral mechanisms. While the peripheral phase is one of adrenergic blockade, the nature of the central mechanism is less clearly defined but is manifested therapeutically by a depression of tone, mainly arteriolar, in various vascular beds. Clinically these

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<sup>\*</sup> Supplies of the alkaloids used in this study were obtained through the courtesy of Sandoz Pharmaceuticals, New York.

mechanisms complement each other to lower systemic blood pressure and to increase peripheral blood flow. Moreover, the hydrogenated alkaloids differ fundamentally from their parent (natural) alkaloids in that they have no uterotonic or vasoconstrictor action and exhibit a more powerful adrenergic blocking activity.

In 1926, Thiel<sup>10</sup> presented evidence for the therapeutic effect of ergotamine tartrate in glaucoma. Rationale for its trial was based on earlier observations in animals to the effect that extirpation of the superior cervical ganglion was associated with a fall in intraocular pressure. It was thought, therefore, that similar effects would be operative if sympathetic blockade was accomplished pharmacologically. Moreover, there is good evidence to suggest that sympathetic innervation may have some bearing not only on vascular diameter but also on vascular permeability. Thus, Ascher13 and Kajikawa13 showed that unilateral extirpation of the superior cervical ganglion protected the corresponding conjunctiva against a mustardinduced conjunctivitis.

About 10 years ago, I attempted to substantiate Thiel's work, but results were equivocal and further studies were abandoned. As a result of the availability of the newer and more effective ergot derivatives, and stimulated by a recent report of Christensen and Swan<sup>13</sup> on the effect of dibenamine in acute glaucoma, I decided to reinvestigate the possible effect of one or several of the ergot derivatives. Observations were first made with dihydroergocristine and subsequently extended to a mixture (CCK 179) in equal parts of the three hydrogenated alkaloids of the dimethylperuvic acid series.<sup>14</sup>

## CLINICAL OBSERVATIONS

These drugs were administered to 29 patients. Of these, 17 had chronic simple glaucoma and 12 had acute congestive glaucoma. The latter group included three cases of secondary glaucoma (thrombosis of the central retinal vein, traumatic hyphemia, and iridocyclitis).

The results obtained were strikingly uniform. In chronic simple glaucoma, the drug did not lower the tension nor did it produce any other demonstrable effect on the eye. Even tensions as high as 60 and 70 mm. Hg (Schiøtz) were not affected.

In the presence of pain and congestion, no matter what the cause of the ocular hypertension, the intravenous administration of the drug resulted in almost immediate relief of pain and in a lowering of ocular tension by an average of 30 percent. One patient (H. S.) with bilateral glaucoma simplex showed no response to the drug on two different trials; on one occasion, however, when seen during a subacute congestive attack with pain and tension of 50 mm. Hg, the drug brought about a lowering of tension to 35 mm. Hg and immediate relief of pain.

The two preparations used, namely DCS 90 and CCK 179, gave essentially similar results; the latter, which is a mixture of three substances, being somewhat more effective.

The first one or two administrations are usually more efficacious than subsequent ones. Increasing the dosage does not influence the effectiveness of the drug. The drug was used in amounts varying between 0.25 and 1.0 mg. In nearly all cases, a dose of 0.3 mg. (corresponding to 1 cc. of CCK 179) is adequate for intravenous administration. It may be administered at intervals as short as four hours; but usually, one or two injections a day suffice in controlling pain.

The drug is relatively harmless and is generally well tolerated. Occasionally, one may encounter an excessive drop in blood pressure. This occurred in only one case of the present series. The patient, a 60-year-old man (L. Y.), had an acute congestive attack of glaucoma of his left eye on which a cyclodialysis had been performed one year previously for chronic simple glaucoma. This patient also suffers from pernicious anemia, with posterior column degeneration, and diabetes. Fol-

lowing an intravenous injection of 0.3 mg. of CCK 179, the tension dropped from 70 mm. Hg to 25 mm. Hg, while the blood pressure dropped from 120 systolic to 80 systolic, the pulse becoming imperceptible. This hypotensive effect was short lasting, the blood pressure returning to 110 after 20 minutes. The ocular tension also rose, but remained at 49 mm. Hg. Since this attack was followed by two subacute attacks within a few days, an iridencleisis was eventually performed.

In order to observe the clinical action of these substances under more or less controlled conditions, a patient was selected whose eye was doomed to enucleation anyway, so that neither a delay in treatment nor the omission of miotics could affect the eventual outcome of the case.

#### CASE REPORT

Mrs. C. D., age 78 years, had a thrombosis of the central retinal vein of the left eye, which, after several weeks, led to a congestive glaucoma with ocular tension of 90 mm. Hg (Schiøtz), pain, and loss of light perception. Pilocarpine hydrochloride (two percent) aggravated the pain without influencing the tension. Enucleation seemed inevitable.

Within five minutes after the intravenous administration of 0.25 mg, dihydroergocristine, the patient was free of ocular pain and of nausea and remained so for 24 hours, or until the next injection of the drug. The tension dropped from over 89 mm. Hg to 65 mm. Hg in six hours and reached 59 mm. Hg after 24 hours. At this time, administration of 0.5 mg, dihydroergocristine resulted in a further reduction of tension to 45 mm. Hg after five hours. The relief from pain continued.

On the following day (third day of treatment), no further lowering of tension was noted, even though 1.0 mg. of the drug was administered.

On the fourth day, 10-percent neosyn-

ephrin was instilled in the eye in addition to the intravenous administration of 0.5 mg. of dihydroergocristine. The tension fluctuated between 51 and 68 mm, Hg and the patient complained of a recurrence of the pain in and around the eye. This was further aggravated by the use of pilocarpine (two percent).

The tension also continued to climb and soon reached its original level. Repeated administration of the drug failed to bring about even temporary improvement. An iridectomy was performed. In the absence of subjective improvement after the operation, the eye had to be enucleated.

The response of the blood pressure paralleled that of the ocular tension. From an original level of 185/94 mm. Hg it dropped to 168/78 mm. Hg after six hours, to reach a new low of 148/78 mm. Hg, five hours after the second dose of the drug. During the subsequent course, it fluctuated between 140/74 and 168/92 mm. Hg and showed no consistent relationship to repeated injections of the drug. As previously mentioned, the drug was used in this patient not with a view toward effecting a cure, but in order to observe its action without its being masked by other therapeutic agents.

#### DISCUSSION

Aside from the value of these drugs in the therapy of glaucoma, the clinical and pharmacologic observations made thus far would seem to justify the tentative postulation of certain general concepts regarding the pathogenesis of glaucoma.

1. Chronic simple glaucoma differs in its pathogenesis from congestive glaucoma.

Congestive glaucoma, whether primary or secondary, is associated with a sympathetic crisis and probably with vasoconstriction in some portion of the vascular bed.

The pain of congestive glaucoma may be mediated via the sympathetic pathways and is relieved by an adrenergic blocking agent of the hydrogenated ergot group.

#### SUMMARY

To summarize briefly, the hydrogenated alkaloids of ergot were found to be of value in the treatment of congestive glaucoma, both primary and secondary. Following are some of the indications for their use:

1. For controlling the pain; it is interesting to note in this connection that these substances have been reported to relieve the pain associated with herpes simplex and herpes zoster.18

2. In cases in which miotics produce insufficient or no lowering of tension.

3. To bring about a partial reduction of tension when miotics are not used or are contraindicated, as in most cases of secondary glaucoma.

4. Preparatory to operation for acute glaucoma, when even a slight lowering of tension helps materially in the technical execution of the operation and in the prevention of complications. For this purpose, the drug should be administered two hours before operation.

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# ALLOXAN DIABETES AND THE LENS\*

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Alterations in the structure of the crystalline lens in diabetics were first observed by Saunders,<sup>1</sup> in 1798, and in the next 50 years reports of diabetic cataracts became common. In a study of 76 cases of ocular complications of diabetes, Gradle<sup>2</sup> found that over 50 percent showed cataractous changes in the lens. However, estimates of the incidence of cataracts in diabetes are prone to error because of the common occurrence of senile changes in the older diabetic. Thus, any clinical study of the etiology of diabetic cataract is of necessity limited by the difficulty in accurately diagnosing these cataracts.

In spite of this limitation, a host of theories have been forwarded to explain the occurrence of diabetic cataracts. The most attractive theory from the standpoint of simplicity relates cataract formation to the hyperglycemia found in diabetics. Thus, von Graefe<sup>a</sup> speaks of a poisoning of the lens by glucose. Kirby and others,4 however, could detect no toxic action of glucose on isolated lens epithelium until a concentration of 578 mg, percent was reached; and Gradle<sup>2</sup> points out that very often cataract formation is independent of the hyperglycemic level in diabetics. On the other hand, Bellows and Rosner<sup>5</sup> showed that in glucose solutions the lens capsule undergoes a decrease in permeability.

A second theory of cataract formation in diabetics is that the opacification is dependent on osmotic variations between the lens and aqueous humor, Unfortunately exceedingly high concentrations of glucose are essential for the formation of cataracts, concentrations that are 50 times that found in normal aqueous and about 20 times that in diabetes.

\* From the Department of Ophthalmology, Northwestern University Medical School. A third theory, postulated as early as 1854 and more recently championed by Goldschimdt<sup>7</sup> and Krause,<sup>8</sup> incriminates the acidity of the aqueous in diabetes as the cause of cataract formation. Krause believes that a local acidity of the lens may cause death of the lens fibers, thus predisposing to proteolytic decomposition. Another theory is based on deranged carbohydrate metabolism with accumulation of toxic products,<sup>9, 10</sup> However, accumulation of acid bodies or other toxic products in the lens has never been unequivocally established.

With the development of mechanisms for producing diabetes experimentally, it has become possible to investigate more intensively the formation of diabetic cataracts. One method is the surgical extirpation of the pancreas. For example, Foglia and Cramer<sup>11,12</sup> removed 95 percent of the pancreas in rats and found that cataracts developed in all rats in 50 days. If 80 percent of the pancreas were removed, cataracts took 200 days to develop and were not so severe. It would thus appear that the formation of cataracts varies directly with the severity of the diabetes.

A second experimental method for the production of diabetes is the injection of anterior pituitary extracts. Dohan¹³ has shown that injection of such extracts causes destruction of the islands of Langerhans and continued administration results in permanent diabetes.

The most recent and most convenient method of producing diabetes was discovered by Dunn, Sheehan, and McLetchie, in 1943, who reported that alloxan administered intravenously in rabbits gave rise to microscopic lesions of the islets of Langerhans. They reported that initially there was a hyperglycemia followed by a hypoglycemia which resulted in death in 12 to 24 hours.

They then suggested a search for animals which would survive with diabetes. This was rapidly accomplished by Dunn, 15 as well as numerous other workers 16, 17 who produced permanent diabetes in rabbits, 18-20 rats, 21-23 and the dog, 17, 24

The complications of diabetes as produced by alloxan have been described by various workers and these complications are ably reviewed by Lukens. <sup>28</sup> Of immediate interest are the ocular complications that develop after the administration of alloxan, Bailey and his group <sup>28, 27</sup> showed that rabbits given 200 mg, of alloxan per Kg, developed cataracts in 4 to 6 weeks. The changes occurred chiefly subcapsularly and in the posterior cortex, Of 15 rats given 200 mg, of alloxan per Kg., diabetes developed in 12, and of this group two developed cataracts.

Cataracts were also reported by other workers<sup>18, 28-30</sup> as a complication of diabetes, although Kennedy and Lukens<sup>21</sup> observed no cataracts in 11 diabetic rabbits for more than six weeks.

Lewis, Moses, and Schneider<sup>29</sup> report cataracts as early as the sixth week in rats and at eight weeks in rabbits, although administration of insulin seems to delay the onset of the cataracts.<sup>27</sup>

The lenticular opacities developing after alloxan diabetes seem to be identical with those produced by pancreatectomy<sup>11, 12</sup> and with the diabetic cataract seen in man.<sup>27</sup>

The mechanism of alloxan action and the pathogenesis of the diabetes so produced have been the object of an intensive research program. Jacobs, 32 in 1937, first described the hypoglycemic action and since then it has been shown that this is only one phase in the process leading to permanent diabetes.

Immediately after the injection of alloxan a hyperglycemia develops. Dunn, Sheehan, and McLetchie<sup>14</sup> state that this is an adreno-sympathetic system response. This has been borne out by Duff<sup>38</sup> and Goldner and Gomori<sup>34</sup> who abolished the initial hyperglycemia by adrenalectomizing rabbits and rats. Following this transient hyperglycemia there is a hypoglycemic phase that has been

attributed to the liberation of insulin from destroyed islet cells. 85, 30 If death does not occur during this hypoglycemic phase, then permanent diabetes develops in 24 to 48 hours which markedly resembles human diabetes in its response to insulin, complications, and microscopic picture.

The action of alloxan occurs in the very first few minutes of its introduction into the body for Gomori and Goldner<sup>87</sup> have shown that clamping off the blood supply to the pancreas for 1 to 6 minutes, after alloxan is given, protects the animal against diabetes. Furthermore, in these animals there is no beta-cell degeneration visible in the islets of Langerhans.

Bailey, Bailey, and Hagan<sup>27</sup> followed the histologic changes in the pancreas very closely and they report that loss of granules was evident in the beta cells five minutes after injection of 200 mg./Kg. of alloxan. In 3 to 6 hours no normal beta cells were evident and by six hours infiltration of polymorphonuclear leukocytes and wandering cells was occurring.

In searching for an explanation of the action of alloxan it was found that in 1930 Labes and Freisburger<sup>38</sup> had reported the affinity of SH groups for alloxan, and in 1937 DeCaro and Rovida<sup>30</sup> showed that the injection of 200 mg./Kg. of alloxan intraperitoneally in rats was followed by a drop of liver glutathione to 17 percent of normal and intestinal glutathione to 42 percent of normal.

In 1946, Lazarow<sup>40</sup> showed that glutathione, given before or with or within three minutes after intravenous alloxan, protected rats against the diabetic effect of the alloxan. Cysteine acted in a similar fashion and Lazarow postulated a protective effect of the sulfhydryl group.

Glutathione and other compounds were then studied by numerous workers and it was found that besides glutathione and cysteine, epinephrine,<sup>41</sup> nicotinic acid,<sup>42</sup> methylene blue,<sup>43</sup> tocopherol,<sup>44</sup> and BAL<sup>45-47</sup> all protected against the action of alloxan. Furthermore, Leech and Bailey<sup>48</sup> showed

that blood glutathione falls rapidly upon injection of alloxan but returns to normal in a short time.

Bruckmann and Wertheimer<sup>49</sup> similarly showed a 45 percent drop in blood glutathione two minutes after injection of alloxan, but were unable to find any decrease in the glutathione levels of the pancreas, liver, and kidney 10 minutes after such an injection.

The mechanism of this alloxan-glutathione reaction has been the object of much research in recent years. Archibald<sup>80</sup> has shown that glutathione reacts with alloxan to form dialuric acid, a nondiabetogenic substance as follows:

$$HN - C = O$$
 $O = C$ 
 $C = O + 2 GSH$ 
 $HN - C = O$ 
 $Glutathione$ 
 $Glutathione$ 

In addition to this reaction Lazarow and his group believe that a glutathione alloxan compound is formed. 51, 83 They have shown that, when equal quantities of alloxan and glutathione are mixed, a new peak at 305 millimicra becomes visible spectroscopically. Lazarow postulates that this new addition compound may be the diabetogenic one.

The basic underlying mechanism of sulfhydryl (glutathione) protection against the diabetogenic action of alloxan is still a debatable one. However, the importance of the SH group in intermediary carbohydrate and protein metabolism has been amply proved by various workers. Barron and Singer\*a have shown that glutathione can reactivate completely enzyme systems poisoned by various sulfhydryl binders. They conclude that glutathione acts by maintaining the SH group in the enzyme in its reduced form, which is apparently essential to its activity.

It is highly probable that a similar mechanism exists in the lens, particularly in the light of the high concentration of reduced glutathione reported in the lens. The average value appears to be about 300 mg./100 gm. of tissue.<sup>84,88</sup> In addition to its high concen-

tration there is further evidence for the importance of glutathione in the lens. A loss of glutathione has been reported in senile cataract<sup>50</sup> and more significantly a similar loss has been reported in galactose cataracts, such decreases occurring before any opacification was visible.<sup>57, 58</sup>

Adams, <sup>89</sup> in a remarkably fine paper in 1925, showed that the lens contained a balanced oxidation-reduction system between glutathione and a thermostable substance whose active component she believed to be B-crystallin. Using fresh lenses Adams showed that the addition of small amounts of glutathione to the lens increased 0<sub>2</sub> uptake 100 percent.

The foregoing considerations as to the importance of glutathione in the lens and the reported sulfhydryl affinity of alloxan induced us to explore the effect of alloxan in diabetogenic doses on the glutathione content of the lens.

In addition to making these chemical observations it was thought advisable to examine the lenses with the slitlamp and in a certain number of cases to make histologic preparations of the excised lenses.

#### METHODS

For the microscopic studies, rats and rabbits were given 200 mg. of alloxan per Kg. and at weekly intervals after the administration, the eyes were examined with the ophthalmoscope and slitlamp. At various times, lenses were removed, fixed, imbedded in celloidin, sectioned, stained, and studied.\*

For the chemical studies, only adult rabbits were used. This was done to avoid the pooling of lenses necessary to obtain valid data from rats. Under sodium pentobarbital anesthesia, one eye was enucleated, the lens

Histologic preparations were made by Dr. H. Reingold.

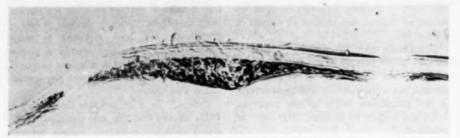


Fig. 1 (Bellows and Shoch). Photomicrograph of alloxan diabetic cataract in the rat, showing proliferation of subcapsular epithelium. (From Bellows, Reingold, and Bell: Unpublished data.)

carefully removed, weighed, and ground with 10-percent trichloracetic acid. The precipitate was centrifuged and the glutathione content of the lens determined. This represented the control value of glutathione. At the same time, a blood sample was drawn from the ear and a control blood glucose level was obtained.

Immediately after this alloxan monohydrate (Eastman) in doses of 200 mg, per Kg, was injected into an ear vein. At intervals of time ranging from 15 minutes to five

Fig. 2 (Bellows and Shoch). Photomicrograph of alloxan diabetic cataract in a rabbit, showing irregularity of the nuclear bow. (From Bellows, Reingold, and Bell: Unpublished data.)

days, the remaining lens was removed and the glutathione concentration determined. At the time of this second enucleation, the blood glucose level was again determined.

Methods used were as follows:

For blood glucose a zinc hydroxide precipitation—phosphotungstic acid method was used.\*

Glutathione was determined by the Benesch and Benesch modification<sup>60</sup> of Kolthoff's amperometric titration method for mercaptans.<sup>61</sup>

The method is primarily a titration of SH groups with Ag\* ions at a rotating platinum electrode. For a complete discussion of the principles and methods involved, the reader is referred to the papers of Kolthoff and the Benesches.

#### RESULTS

#### A. MICROSCOPIC

The earliest changes seen in rats with the slitlamp occurred in 1 to 2 weeks. These consisted of an accentuation of the anterior Y suture with a narrow zone of lens fibers of increased reflection surrounding it. In the same area, at a later date, there appeared to be clumps of opacities on the limbs of the Y producing a triradiate cataract. Minute punctate opacities became numerous in the external lens layers. Later dense opaque plaques appeared subcapsularly which on section proved to be formed by reduplication

Method developed by O. Rupe of the Chemistry Department, Northwestern University Medical School, to be published.

of the lens epithelium which in some areas was as much as 10 cell layers thick (fig. 1).

Changes in the structure of the rabbit lens were evident at the first weekly examination after alloxan administration. These consisted of the appearance of minute vacuoles in the extreme equatorial region, visible only with intense illumination and a magnifying loupe. This change occurred only in rabbits made diabetic by alloxan and was not seen in those rabbits that did not become diabetic as a result of alloxan administration. In those rabbits that survived, the more obvious cortical changes appeared later. Figure 2 shows the histologic changes occurring in an incipient cataract. This consists chiefly of a disturbance of the nuclear bow (fig. 2),

## B. CHEMICAL

The results obtained are tabulated in Tables 1 through 6. In determining glutathione in rabbit lenses there was found to be a marked variation from animal to animal, but remarkable consistency from eye to eye in the same animal. For this reason, one

lens was always extracted first as a control.

A total of 40 rabbits was used. After the alloxan injection, these rabbits were given 100 cc. of five-percent glucose subcutaneously and glucose was put into their drinking water. They did not receive any insulin because it was desired to produce diabetes and its complications in these animals as soon as possible. Of the 40 rabbits, 12 died in the hypoglycemic phase before the postalloxan lens could be analyzed. The glutathione values for these 12 lenses plus the 28 control lenses from the experimental group ranged from 158 to 371 mg./100 gm. of tissue with a mean of 263 ± 9 mg./100 gm.\*

The glutathione values for the experimental group of 28 rabbits is tabulated in Tables 1 through 6.

Two rabbits inadvertently were allowed to live beyond the maximum five-day period of the experiment and gave the results shown in Table 7.

\* 
$$\pm$$
 9 = standard deviation of mean =  $\frac{1}{\sqrt{n-1}}$ 

TABLE 1 Effect of 200 mg. alloxan/Kg, on lens glutathione after short intervals of time

					e mg./100 gm.	Blood Glucose mg.	
Rabbit #	after Alloxan - that Lens was Extracted	Control	Post-Alloxan Value	Control	Post-Alloxar		
	(minutes)						
1	0	332	330				
21	15	227 253	234 264	114	116		
30	60	318	314	114	110		

TABLE 2
Lens glutathione 24 hours after injection of 200 mg. alloxan/Kg.

	Glutathione	Glutathione mg./100 gm.		lood Glucose mg.%	
Rabbit ∮	Control	24 hr. after Alloxan	Control	24 hrs. afte Alloxan	
14	190	185		-	
36 39	264	255 208	91	86 88	
39	212	208	95	88	

TABLE 3

Lens glutathione 48 hours after injection of 200 mg. alloxan/Kg.

	Glutathione	mg./100 gm.	Blood Glucose mg.%	
Rabbit /	Control	48 hrs. after Alloxan	Control	48 hrs. after Alloxan
3	322	306	-	-
4	371	369	95	159
15	195	191	89	178

TABLE 4
Lens glutathione 72 hours after injection of 200 mg. alloxan/Kg.

	Glutathione	mg./100 gm.	Blood Gl	ucose mg.%
Rabbit #	Control	72 hrs. after Alloxan	Control	72 hrs. after Alloxan
12	311	143 102 224 170		
18	191	102	123	511
22	246	224	88 101	452
18 22 33	321	170	101	432
	248 - 80	460 - 26		
Mean	p = 0.05	$160 \pm 26$		

TABLE 5
LENS GLUTATHIONE 96 HOURS AFTER INJECTION OF 200 MG. ALLOXAN/KG.

	Glutathione n	ng./100 gm.	Blood Gl	ucose mg.%
Rabbit #	Control	96 hrs. after Alloxan	Control	96 hrs. after Alloxan
8	292	93	84	442
11	265	94		4-00
27	264	140	103	404
29		100	.112	416
35	238	126	112	688
11 27 29 35 40 — Mean	186 238 240	140 100 126 94	96	404 416 688 533
ines	-	-		
Mean	$248 \pm 15$ $p = 0.001$	125 ± 11		

TABLE 6
Lens glutathione five days after injection of 200 mg./alloxan/Kg.

	Glutathione n	ng /100 gm.	Blood Glucose mg.%	
Rabbit #	Control	5 days after Alloxan	Control	5 days after Alloxan
5	362	114 100 109 147 217* 103	-	_
10 20	222	100	-	_
20	328	109	88 104 92	612 512 128*
24	301	147	104	512
37	259	217*	92	128*
24 37 38	362 222 328 301 259 274	103	94	458
manus.	-	Military Co.		
Mean	$291 \pm 21$ $p = 0.001$	115±8		

<sup>\*</sup> These rabbits did not become diabetic and are excluded from calculation of mean.

### Discussion

# A. MICROSCOPIC STUDIES

The early changes at the suture lines described in the rat are best explained by water absorption. The water appears first in the suture lines accentuating them and then by diffusion into the adjacent layers produces the increased reflection and opalescence already noted. With the dissolution of the lens fibers, insoluble protein particles (morgagnian bodies) and lipids are precipitated and form the opacities already described. The

plained by the fact that the method used by us determines only reduced SH groups even in the presence of Cl ion, ascorbic acid, Fe<sup>\*\*\*</sup> ion, and other groups. Accordingly, we feel that our lower figure is a truer estimate of the glutathione content of the normal rabbit lens.

It is apparent from our figures that there is no immediate combination of alloxan with glutathione in the lens as has been reported for blood. The glutathione decrease did not occur until 72 hours after the injection of alloxan by which time alloxan has completely

TABLE 7

LENS GLUTATHIONE AFTER INJECTION OF 200 MG. ALLOXAN/KG.

Th 111. d	Days after	Glutathione		Blood	Glucose
Rabbit ∉	Alloxan	Control	After Alloxan	Control	After Alloxan
25	12	166	55	105	511
17	25	158	151*	112	76*

\* These rabbits did not become diabetic and are excluded from calculation of mean.

dense subcapsular plaques are produced by epithelial proliferation as illustrated.

The vacuolization described in the rabbit is probably the earliest lesion in experimental diabetic cataract. From this, it would appear that the most vulnerable fibers are the youngest ones developing at the equator. This is substantiated by the changes in the nuclear bow illustrated in Figure 2. It is possible that these changes also occur in human diabetes but have been overlooked because of the difficulty in examining this region with the slitlamp. The use of oblique illumination, a binocular loupe, and a widely dilated pupil in examining young diabetics should either substantiate or disprove this hypothesis.

## B. CHEMICAL STUDIES

The value obtained for glutathione in normal rabbits' lenses  $(263 \pm 9 \text{ mg}, \%)$  agrees with many figures in the literature although it is 80 to 100 mg, lower than that obtained by averaging the available figures. We feel that our lower figures are partially ex-

disappeared from the body and destruction of the beta cells and the islets of Langerhans is well established.

Furthermore, if we assume that diabetes does not exist until a blood glucose level of over 200 mg. percent is reached it becomes apparent that the glutathione decrease occurs only after the establishment of the diabetes (tables 3 and 4). We may, therefore, conclude that the drop in lens glutathione is due not to the alloxan but to the diabetes that the alloxan produces.

This is further borne out in the cases of rabbits No. 17 and No. 37 which did not develop diabetes after alloxan and did not show any decrease in lens glutathione. This parallels the observation that those animals receiving alloxan that did not develop diabetes did not show gross or microscopic lens changes.

Although it cannot be concluded from our experiment that the loss of glutathione is the etiologic factor in the development of diabetic cataract, it is evident that this loss plays a role in its pathogenesis. The decreased

glutathione concentration may be explained either on the basis of direct oxidation of it which in turn causes a loss of its protective action on the enzyme proteins of the lens or it may be that it is the SH group in the protein that is oxidized which then exhausts the available free glutathione in an attempt to reactivate the enzyme.

## Conclusions

1. The earliest lesion in alloxan diabetic cataract is the appearance of minute vacuoles at the equator. This occurred within a few days in the rabbit. This is probably due to the fact that the young lens fibers are the most vulnerable in experimental diabetic cataract. In the rat, the earliest change appears at the suture lines and adjacent lens fibers. These were followed by the formation of the usual opacities (punctate, radiating, and so forth) which are usually ascribed to coagulation and liquefaction of lens fibers.

2. The average glutathione content of the adult rabbit lens as determined by amperometric titration is  $263 \pm 9$  mg./100 gm. lens tissue.

 Alloxan does not cause a decrease in lens glutathione because the first loss in glutathione occurs long after the alloxan has been detoxified and excreted from the body.

4. Glutathione in the lens shows a decrease of 40 to 60 percent occurring, at the earliest, 72 hours after injection of alloxan, and this decrease is dependent on the existence of a severe diabetes.

If diabetes does not develop as the result of alloxan injection, the decrease in lens glutathione does not occur and cataract does not develop.

 The loss of glutathione appears to be an important factor in the pathogenesis of alloxan diabetic cataract.

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# OCULAR MANIFESTATIONS OF INTRAVENOUS TETRAETHYL AMMONIUM CHLORIDE IN MAN\*

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In the course of evaluating various curariform muscle relaxants in man, their lack of effect upon the autonomic structures of the eye was noted. As a companion study, the effect upon the eyes of tetraethyl ammonium chloride (T.E.A.) was investigated because of its known sympathetic and parasympathetic ganglionic blocking action.

#### PHARMACOLOGY

T.E.A. (Etamon Chloride, Parke Davis) is a quaternary amine having the structural formula:

$$C_2H_3$$
 $N = C_1$ 
 $C_2H_3$ 
 $C_2H_3$ 

N(C<sub>2</sub>H<sub>3</sub>)<sub>4</sub>Cl. It has been classified by Nickerson and Goodman<sup>7</sup> as one of several drugs blocking autonomic effector systems innervated by cholinergic preganglionic nerves.

Acheson and Moe<sup>1</sup> showed that T.E.A. blocked the parasympathetic ganglia. They demonstrated that it eliminated the vagal inhibitory action on cardiac activity in dogs. Studying the nictitating membrane of cats, Acheson and Pereira<sup>2</sup> demonstrated the sympathetic ganglionic blocking action of T.E.A. upon the superior cervical ganglion.

Heymans and Hoorens,<sup>8</sup> working with dogs, showed that topical T.E.A. (1 to 10 percent) had no effect upon pupillary size and action. They reported that small subconjunctival and intraocular injections produced a slight mydriasis, while intravenous T.E.A. (10 to 15 mg./Kg.) was an active mydriatic. The latter reduced the myosis of either D.F.P. (di-isopropyl fluorophosphate) or eserine, but did not suppress the myosis of acetylcholine or pilocarpine.

Lyons and co-workers4 demonstrated the

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combined sympathetic and parasympathetic ganglionic blocking action of T.E.A. in man. This drug has been used as a diagnostic aid to investigate the feasibility of sympathectomy in essential hypertension.<sup>4</sup>

# PROCEDURE

Seven volunteer subjects, all healthy males (aged 23 to 30 years), were selected in order to study the effects of T.E.A. on the normal human eye. The subjects remained recumbent during the entire experiment. Over a four-minute period, 500 mg., or an average of 7.0 mg. per Kg. of body weight, of the drug were administered intravenously. Two drops of the various miotics studied were instilled upon the cornea one-half hour before administration of T.E.A.

## Systemic effects

A metallic taste in the mouth, paresthesias, and sensations of coldness and/or burning of hands and feet were reported. It was found that, in the prescribed dosage, there was throughout the experiment no significant effect on striated muscles. The hand

noticeably with the radial pulse becoming difficult to palpate. Vasopressors were not necessary as the hypotension was immediately rectified by having the subject lie down again. As a precautionary measure against hypotension, all ocular observations were made with the subject recumbent. The time interval from start of injection to full recovery without clinically discernible aftereffects was in all cases one hour or less.

# OCULAR MANIFESTATIONS

- No alteration in the motility of the extraocular muscles occurred.
- No significant change was observed in the near point of convergence.
- Slight ptosis was present in one experiment only.
- Measurements with the Hertl exophthalmometer revealed no change in ocular prominence.
  - 5. Corneal sensitivity was unaffected.
- 6. Tonometry (Schiøtz) revealed a rapid and profound drop in intraocular pressure with a gradual return to the pre-injection level in 40 to 60 minutes. Examples of this reduction in tension are:

	(	Subject P.	C.)		(Subject J.	D.)
Time	O.D.	O.S.	B.P.	O.D.	O.S.	B.P.
Control	22	23	118/82	24	25	128/78
5 min.	14	17				118/76
10 min.	13	16	118/86	14	16	122/84
20 min.	14	17	116/84	16	17	122/80
30 min.	16	19	116/86	19	23	122/84
40 min.	16	19		23	25	
50 min.	17	19		23	25	126/84
60 min.	20	22	116/84	23	26	

grip, as indicated by the dynamometer, was used to reveal the status of the skeletal muscles. This did not vary significantly from the control level. The pulse rate increased an average of 24 beats per minutes while the systolic and diastolic blood pressures decreased an average of 9.5 and 5.1 mm. of Hg, respectively.

For the purpose of this study the subject was allowed to sit up at the height of the systemic effect and the blood pressure dropped The maximum reduction of intraocular pressure was reached 10 minutes after the start of injection (fig. 1, A and B).

The pupils dilated to a midposition with some anisocoria and in several subjects assumed a catlike elliptical shape.

8. Pupillary reaction was markedly diminished. The reponse to light was slight and sluggish, and the reaction to accommodation was temporarily lost. Dark adaptation did not cause the pupils to dilate further.

Full paralysis was not obtained with the dosage used.

9. The near point of accommodation receded to beyond 20 feet in approximately eight minutes after the start of injection; this depth of cycloplegia was present for the next 8 to 10 minutes. Cycloplegic retinoscopy and refraction were easily accomplished with the subject lying on his side. Monocular vi-

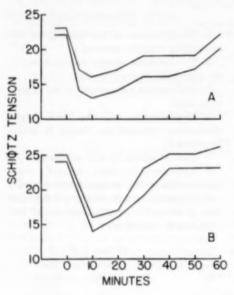


Fig. 1 (Drucker, Sadove, Unna). Reduction of intraocular pressure following intravenous administration of T.E.A. (over a four-minute period starting at zero (0) time) to normal subjects: (A) P. C., (B) J. D.

sion in every case was correctible to 20/20+ with the full cycloplegic correction. An addition of +3.0D., O.U., allowed J1 to be easily read at 33 cm. The average residual accommodative range was 10.6 cm.

Postcycloplegic examinations were made one hour after injection with the usual subtraction of +0.5D, to +1.0D, being necessary to give corrected vision of 20/20+. Examples of refraction findings were as follows:

Subject R. C. (hyperope):

Vision without glasses:

O.D., 20/25-O.S., 20/25-

Net T.E.A. (retinoscopy):

O.D., +3.25D, sph.  $\bigcirc +0.5D$ , cyl. ax.  $90^{\circ} =$ 20/20+

O.S., +3.25D. sph.  $\bigcirc +0.5D$ . cyl. ax.  $90^{\circ} =$ 20/20+

Post T.E.A. cycloplegia:

O.D., +2.25D. sph.  $\bigcirc +0.5D$ . cyl. ax.  $90^{\circ} =$ 20/20+

O.S., +2.25D. sph. C +0.5D. cyl. ax. 90° = 20/20+

Subject D. McF. (emmetrope)

Vision without glasses:

O.D., 20/20+ O.S., 20/20+

Net T.E.A. (retinoscopy):

O.D., +1.0D. sph. = 20/15-

O.S., +1.25D. sph. = 20/15— Post T.E.A. cycloplegia:

O.D., +0.5D. sph. = 20/15 O.S., +0.75D. sph. = 20/15

Subject J. N. (myope)

Vision without glasses:

O.D., 20/200-

O.S., 20/200-

Net T.E.A. (retinoscopy): O.D., -2.25D. sph.  $\bigcirc -0.75D$ . cyl. ax.  $180^{\circ} =$ 

20/20+

20/15+

O.S., -2.75D, sph.  $\bigcirc -0.5D$ , cyl. ax.  $180^{\circ} =$ 20/20+

Post T.E.A. cycloplegia:

O.D., -2.25D. sph.  $\bigcirc -0.75D$ . cyl. ax.  $180^{\circ} =$ 

O.S., -2.75D. sph.  $\bigcirc -0.5D$ . cyl. ax.  $180^{\circ} =$ 

10. Ophthalmoscopy revealed no changes.

11. Myosis caused by topical instillation of eserine salicylate (0.5 percent) or diisopropyl fluorophosphate (D.F.P.) (0.1 percent) was reduced transiently by a 500mg. dose of intravenous T.E.A., while the myosis caused by similarly administered carbachol (Carcholin, Merck) (1.0 percent) or pilocarpine (2.0 percent) was unaffected. Tearing was simultaneously suppressed.

12. For comparison with T.E.A., a recently introduced<sup>8</sup> and reportedly potent<sup>5</sup> autonomic blocking agent, pentamethylenebis-(triethyl ammonium iodide), I(CH<sub>3</sub>)<sub>3</sub>N-(CH<sub>2</sub>)<sub>5</sub>-N(CH<sub>3</sub>)<sub>3</sub>I, herein titled C5, was tested intravenously on two subjects. In 50mg, doses administered over a five-minute interval, it was found to have none of the ocular effects of T.E.A. except moderate intraocular-pressure reducing qualities which appeared to be of a longer duration.

# COMMENTS

T.E.A. (a quaternary amine) acts as an autonomic ganglionic blocking agent. All observations herein reported may be explained by this accepted mode of action. The midposition to which the pupils dilated can be interpreted as being caused by the blocking effects upon the sympathetic and parasympathetic ganglia.

With regard to the work of Heymans and Hoorens in dogs and the antagonism of T.E.A. toward certain miotics, we found in our subjects that intravenous T.E.A. also provided transient inhibition to the acetyl-choline-mimetic postganglionic action of D.F.P. and eserine upon the iris. It had no effect upon miosis caused by pilocarpine or carbachol which act directly upon the parasympathetic receptor mechanism of the iris.

Blood pressure changes alone were not sufficient to account for the magnitude and rapidity of change of intraocular pressure. One may speculate that we have here another manifestation of local autonomic cholinergic blockade.

From these preliminary findings it is to be suspected that, in selected cases, T.E.A. and C5 may be useful drugs to initiate rapid antiglaucomatous therapy. The place of T.E.A. as an ultrashort-acting, deep cycloplegic in properly selected patients who cannot afford the time and inconvenience of the usual types of cycloplegia is suggested. The combination of cycloplegia and intraocular-

interval, it was found to have none of the ocular effects of T.E.A. except moderate in-

## CONCLUSIONS

Besides lowering blood pressure and increasing the pulse rate, T.E.A. affects ocular structures as an iridoplegic, a partially dilating mydriatic, and an efficient cycloplegic. It produces a rapid and profound reduction in intraocular pressure, but this is of short duration.

Intravenous T.E.A. inhibits the miotic effects of 0.1-percent D.F.P. or 0.5-percent eserine while having no effect upon the miosis of 2.0-percent pilocarpine or 1.0-percent carbachol topically instilled onto the cornea. The extraocular muscles and other striate skeletal muscles were unaffected. The near point of convergence, the ocular prominence, and the fundus showed no significant changes.

These findings were obtained when doses averaging 7.0 mg. per Kg. of body weight were administered intravenously to normal humans over a four-minute period. C5 in the total dosage of 50 mg. administered intravenously over a five-minute interval was found to act on the eyes only as a tension-reducing agent. Further investigation will be necessary to determine the exact status of T.E.A. and C5 with respect to ocular therapeutics.

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# TEMPORAL ARTERITIS AS A CAUSE OF BLINDNESS

REVIEW OF THE LITERATURE AND REPORT OF A CASE\*

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Temporal arteritis is the name given to a local and systemic symptom complex that attacks people between the ages of 55 and 80 years (although Meyers and Lord¹ have reported a case in a patient, aged 22 years). The females outnumber the males 3 to 1.

Local symptoms are pain and tenderness along the course of the temporal arteries, which are red, swollen, nodular, and stenosed. The systemic symptoms consist of fever, malaise, anorexia, and loss of weight. The temperature range is from 99°F. to 103°F., and the cause is unknown.

The diagnostic arteritis of the temporal arteries may appear at any time, from a few days to a few mouths from the onset of symptoms. Leukocytosis averaging 12,000 white blood cells per cc. may occur, and local symptoms vary with the location of inflamed vessels. Disorientation, mental hebetude, and even delirium have been described.

Pathologic examination shows thickening of the arterial wall involving all three coats and narrowing or occlusion of the lumen. The intima is hypertrophied, the media necrotic, and, together with the adventitia, infiltrated with lymphocytes and polymorphonuclear cells. Giant cells in the media are a characteristic feature.

The course may run from a month to nearly three years, and the mortality (as estimated by Crosby and Wadsworth<sup>2</sup>) is about 12.5 percent. Treatment is ineffective, but section of the temporal artery is recommended by some writers, and Roberts and Askey<sup>8</sup> have pointed out that the pain can be controlled by injection of procaine around the affected vessels. Vasodilators are useless.

They and writers immediately following them believed that the arteritis was confined to the temporal arteries; and Johnson, Harley, and Horton,6 in an attempt to explain involvement of the retinal vessels, have suggested a spread of the process from the temporal through the lacrimal branch of the ophthalmic to the central retinal artery. Now, however, it is apparent that the disease is more widespread than was formerly thought, and the process has been found at autopsy to have involved one or more of the retinal, carotid, subclavian, coronary, renal, mesenteric, innominate, iliac, pulmonary, femoral, brachial, and dorsalis pedis arteries.

Even the designation "cranial arteritis" as suggested by Curtis' and others is obviously insufficient in the light of this newer knowledge. Nevertheless, the term temporal arteritis is used here because it describes the presenting and diagnostic findings, and a final designation will probably have to wait until a definite pathologic or etiologic picture emerges.

The reader who wishes to study the general aspects of the disease is referred to the

The first case of temporal arteritis was described in 1930 by Schmidt<sup>4n</sup> of Copenhagen, whose 69-year-old patient (Case 24) had fever, swollen, tender, and occluded temporal arteries, and diminished vision in one eye. This patient had an intracranial aneurysm of the internal carotid artery, and was reported as such, but the temporal arteritis was unmistakable. Even though the article was subsequently published in English,<sup>40</sup> it seems to have escaped the notice of American writers on the disease. They give priority to Horton, Magath, and Brown,<sup>8</sup> who pointed out that this syndrome formed a definite clinical entity.

<sup>\*</sup>From the Institute of Ophthalmology of the Presbyterian Hospital. Presented at the 86th annual meeting of the American Ophthalmological Society, Hot Springs, Virginia, May, 1949.

excellent review by Crosby and Wadsworth.<sup>a</sup>
Contributions published since their work
was completed may be found under the
names of Winblad,<sup>a</sup> Gordon and Thurber,<sup>a</sup>
Broch and Ytrehus,<sup>10</sup> Ricard,<sup>11</sup> Hoyne,<sup>12</sup>
Van Balen and deBruyne,<sup>13</sup> Justin-Besancon,<sup>14</sup> Jennings,<sup>13</sup> Protas and Saidman,<sup>16</sup>
Zeller,<sup>17</sup> and Criep,<sup>18</sup> and also in the bibliography given herewith. The following
case is fairly typical.

### CASE REPORT

History. M. D., a 74-year-old white woman, entered the Presbyterian Hospital, New York, on July 7, 1948. About the middle of the preceding May, she had experienced pain over the left parietal area extending into the occipital region and down into the cervical region on the same side. These pains were mild, infrequent, and transitory at first, but within two weeks they had become severe and had radiated to the left scapular region. She began to lose appetite, and became easily fatigued. Nevertheless, in June, 1948, the patient traveled to England, France, and Italy; and on June 26th, while in Italy, experienced a severe headache over the right parietal and temporal regions radiating over the vertex to the suboccipital area and from there to the right scapular region. When she awakened the next morning there was a "brown veil" over the right eye, and by the following morning this eye was completely blind. The vision in the left eye disappeared in a similar fashion during the next day. Since then she had noticed no change in her condition, but stated that she had lost 15 pounds in weight since she became ill.

The patient had been born in Indiana and lived all of her life in the United States except for about five months in China. She smoked a half pack of cigarettes a day, drank about one and one-half cups of coffee daily, and took only an occasional cocktail. She had had no acute infectious diseases except scarlet fever as a baby. Three immunization injections for typhoid had been given in 1923, and she was vaccinated—apparently with no reaction—in May, 1948, as part of the legal requirements for

her trip.

There were no allergic phenomena, no operations or injuries, and she had never received penicillin nor the sulfonamides. The hearing in the right ear was slightly diminished and had been so for many years, probably as a result of ofitis media. There was no history of respiratory, cardiac, gastrointestinal, genito-urinary, neuromuscular, or emotional disturbance. Her mother had died of pernicious anemia at the age of 62 years, and her father of unknown causes at age 60 years.

Physical examination revealed an obese woman of the stated age. Temperature 100.4°F., pulse 90, respiration 20, blood pressure 150/85 mm. Hg. The patient was pale, exhausted, and the breath slightly

acidotic. The temporal artery on the left side was tender, palpable, and sclerotic.

The nonprotein nitrogen was 29.9, the urine and Kline tests negative. The complete blood count was as follows: red blood cells, 4,450,000; white blood cells, 21,200; hemoglobin, 12.3; polymorphonuclears, 32; lymphocytes, 66; myelocytes, 2; erythrocyte sedimentation rate, 75; sheep cell agglutination, 1—8; serum phosphatase, 2.5; Bodansky units, 1 percent, cephalin flocculation, negative, basal metabolic rate, —9.

Bone marrow aspiration revealed a marked increase in lymphocytes without the morphologic changes seen in mononucleosis. The spinal fluid protein was 25 mg. percent, sugar 71 mg. percent, and spinal fluid—Kline and gold curve—negative. Xray studies of the skull were negative. There was some X-ray evidence of degenerative arthritis of the lumbosacral spine, and calcification was present

in the abdominal aorta.

Examination of the eyes showed no external disease and no evidence of involvement of the external ocular muscles. The pupils were wide and fixed, the media clear except for a few fine posterior vitreous opacities. The arteries were a little smaller, the veins a little larger than normal. There was slight indentation, but actual sclerosis could be graded as no more than one plus. The right disc was badly defined, showing a slightly yellowish pallor, and was not elevated. There was a small area of hemorrhage and a little exudate near the disc at the 7-o'clock position. The left disc was similar, but no hemorrhages or exudates were seen. Vision was no perception of light, each eve.

The patient was given 300 mg. of aureomycin intramuscularly daily for three days with no discoverable effect. She remained in the hospital for 24 days, during which time her headaches subsided but her temperature remained elevated—never lower than 99°F, never higher than 100.6°F. She was discharged to her home with the diagnosis of temporal (cranial) arteritis. The low-grade lymphatic leukemia was considered to be coincidental. She was examined at her home four months later. She felt well but was completely blind. Her pupils were still dilated and fixed, her retinal arteries quite small, and her discs completely atrophic.

### DISCUSSION

#### REVIEW OF LITERATURE

Because so many patients suffering from temporal arteritis have complained of visual disturbances, I have gone through the literature to obtain some idea of the incidence, mode of action, and prognosis of ocular involvement. I have been able to discover some 83 suitable cases, to which my own is added to make 84. Of these, 34 (again including my own case) have contained refer-

ences to involvement of the eyes. These ocular signs and symptoms have varied widely. Horton and Magath10 described merely "retinal phlebitis" in two cases. One case reported by Johnson, Harley and Horton<sup>6</sup> suffered sudden complete blindness in one eye. In the first of these cases, ischemic areas were found along the superior temporal vessels, and there was occlusion of the superior temporal artery with fragmentation of the blood stream. In the second case, the left disc was slightly pale and edematous. There were a few hemorrhages in the superior nasal quadrant, and some exudate between the disc and the macula. In the third case, the discs were pale and edematous,

Jennings's<sup>20</sup> case showed complete obstruction of the left central retinal artery and gradual closure of its fellow.

In Cooke's<sup>21</sup> first case the disc was blurred and pale, and there was a patch of exudate above the macula. In his second case the right disc was pale, the arteries were small, and there was one hemorrhage and a few patches of exudate. In the left eye the disc was edematous and pale. In his third case the arteries were normal but the discs were pale. In his sixth case the right disc was edematous and the left normal at first, although they both became atrophic subsequently. His eighth case showed narrowed vessels with normal discs.

Dick and Freeman's<sup>22</sup> first case had a slightly edematous disc with a small hemorrhage on its surface, and Bain's<sup>23</sup> case showed bilateral peripapillary atrophy.

In Shannon and Solomon's<sup>24</sup> case the discs were edematous and the arteries threadlike. There were a hemorrhage and a few areas of exudate in the right retina.

Post and Sanders's<sup>20</sup> case was normal at the time of the acute systemic attack. Six years later the retinal arteries were sclerosed, and there was periarterial sheathing with enough thickening of the walls to conceal the blood stream. Three areas of silvery exudate were seen below and nasal to the macula. In Curtis's' case the patient became totally blind, but narrowing of the arteries and atrophy did not appear for some weeks.

The case reported by LeBeau and his coworkers<sup>26</sup> became completely blind, showing pale, blurred discs and edema in the posterior pole. In Smith and Greene's<sup>27</sup> first case the patient became blind in the right eye, which appeared normal except for two small hemorrhages near the disc. Eighteen days later the left eye also became blind, but in this eye there was some edema of the disc. Their second case became completely blind in the right eye. The vision in the left eye fell to 20/200, and there was some swelling of the disc, Later the vision returned to 20/25 in this eye, but the disc became pale.

In the first case reported by Crosby and Wadsworth,<sup>2</sup> the patient complained of a cloud over one eye, then the other. The vessels were narrow and segmented, and there were hemorrhages. The patient was totally blind in 15 days and so remained. The

nerves became pale.

The patient in their third case complained of diplopia and became blind in the right eye. The vessels were narrow; and there was a hemorrhage on the disc. In their fourth case there was complaint of a "smoke screen" and the patient became blind in the right eye. The discs were pale, but recovery took place in a week.

The second case reported by Robertson<sup>28</sup> went blind with occlusion of the central artery and fragmentation of the stream. The same phenomenon was observed by W. B. Anderson,<sup>28</sup> whose cases went on to optic atrophy. The case reported by Peltola<sup>20</sup> showed blurring of the right disc with narrowed arteries.

T. Andersen's<sup>31</sup> case had glaucoma, but any connection with the original disease is not clear, and the same may be said of Wolinetz's<sup>32</sup> case, in which he found bilateral cataracts.

The only pathologic report on the optic nerve was given by Cooke and his associates<sup>21</sup> who described the nerves as showing marked softening, and the lumina of the retinal arteries as being obliterated by cellular fibrous tissue.

# EVALUATION OF REPORTS IN LITERATURE

It is now clear that the task of correlating, classifying, and evaluating these findings is difficult indeed. In many cases the eyes were obviously not examined even when the patient had visual complaints. Thus, Cooke and his collaborators<sup>21</sup> speak of "some deterioration of eyesight," Dick and Freeman<sup>22</sup> mention "poor vision in one eye," and Cole<sup>23</sup> speaks of "blurred vision" with no further explanation.

The time of onset of ocular symptoms is not always stated, and the time of examination of the eyes is not always clear. Nor is the ocular follow-up noted in most cases. This is particularly important because the fundi may be normal for a while and the discs may not become atrophic until considerable time has elapsed.

The situation is further complicated by the fact that one pathologic condition was frequently found in one eye, a different one in the other, and, to make matters more confusing, different lesions in the same eye.

Moreover, some of the lesions (such as the diplopia described by Dick and Freeman,<sup>22</sup> Cooke and his co-workers,<sup>21</sup> Crosby and Wadsworth<sup>2</sup> and others, and the ptosis described by Murphy,<sup>24</sup> Cooke and his co-workers<sup>21</sup> and others) were certainly not ocular in origin, although the complaints were of course referred to the eyes. Finally, the advanced age of most of the patients made such sclerotic signs as exudate, arterial narrowing, and hemorrhage much more likely to be found, and such findings as cataract and glaucoma might easily fall into the same category.

Nevertheless, a certain pattern emerges from the confusion. As Wagener<sup>88</sup> has pointed out, the eyes seem to be attacked in two ways. First, a closure of the retinal arteries in the nerve may occur. This may be permanent or, rarely, due to a spasm, in which latter case some vision may be restored. Second, the ischemia may take place behind the entry of the retinal vessels into the nerve, and, in this event, symptoms indistinguishable from an acute retrobulbar neuritis occur. They almost invariably go on to optic atrophy.

This leaves a group of cases that are not fully explained. Wagener<sup>35</sup> calls these the "indeterminate" group.

In the first (occlusive) group, we may place the case of Jennings, <sup>30</sup> Johnson, Harley, and Horton, <sup>6</sup> one of the cases of Cooke and his co-workers, <sup>31</sup> a case of Anderson and his collaborators, <sup>29</sup> and a case of Robertson. <sup>28</sup>

In the second (ischemic-neuritic) group, we may place the case of Dick and Freeman, <sup>92</sup> two cases of Johnson, Harley, and Horton, <sup>6</sup> the case of Shannon and Solomon, <sup>24</sup> three cases of Cooke and his coworkers, <sup>21</sup> Curtis's' case, both cases of Smith and Greene, <sup>27</sup> the case of LeBeau and his co-workers, <sup>20</sup> the case of Peltola, <sup>20</sup> and the case reported here.

The third, or indeterminate, group may be divided as follows:

 Unexplained loss of vision (Dick and Freeman,<sup>22</sup> Johnson—quoted by Horton, and Cole<sup>33</sup>).

Subretinal hemorrhage (Cooke and his co-workers<sup>21</sup>).

3, "Retinal phlebitis" (Horton and Magath<sup>19</sup>), two cases.

 Photophobia (Bain<sup>23</sup> and Crosby and Wadsworth<sup>2</sup>).

 General narrowing (Cooke and his coworkers,<sup>21</sup> Anderson and his collaborators<sup>29</sup> and Crosby and Wadsworth<sup>2</sup>).

6. Periarterial sheathing and macular exudate (Post and Sanders<sup>26</sup>).

 Cataract (Wolinetz and his co-workers<sup>32</sup>).

8. Glaucoma (Anderson<sup>81</sup>).

9. Pressure of aneurysm (Schmidt<sup>4</sup>).

The cases of diplopia and ptosis, being

# TABLE 1 INCIDENCE

				The same of the same
Total number Total number	of cases.	s involved	84 34	40%

# TABLE 2 METHOD OF INVOLVEMENT

1. Occlusion of artery. 2. Ischemic retrobulbar neuritis 3. Indeterminate a. Unexplained loss of vision. 5. Subretinal hemorrhage. 1. C. "Retinal phebitis". 2. d. Photophobia 2. e. General narrowing of arteries 6. Pariarterial sheathing, etc. 7. Pressure of aneurysm. 1. Interpressure of aneurysm. 1. Inte	6 13	18% 38%
h. Questionable (cataract, glau- coma)	15	44%
	34	100%

# TABLE 3 SEQUELAE

		-
Blind in both eyes. Blind in one eye. Various degrees of impairment. Presumable recovery. Uncertain (died, not stated, etc.)	13 9 7 2 3	38% 27% 20% 5% 8%
	34	100%

due to involvement of vessels outside the eye, are not included.

Of the 34 cases of visual disturbance investigated, six were due to closure of the retinal artery, 13 to ischemia of the nerve behind the point of entry of the retinal vessels, and 15 to various other causes. Nine

became blind in one eye, 12 were blind in both eyes, and the rest suffered various degrees of visual impairment. In only two cases did the vision return to normal following more or less short periods of amaurosis. These results are condensed in Tables 1, 2, and 3.

# SUMMARY AND CONCLUSIONS

The literature on temporal arteritis is reviewed with special reference to the effect of the disease upon the eye, and a typical case is reported. It appears from this study that, in 40 percent of cases of temporal arteritis, the eyes may be expected to become involved, chiefly by occlusion of the retinal arteries or their branches, or by the production of ischemia of the optic nerve behind the point of entry of the retinal vessels into that nerve. The eyes may become involved within a few days or as late as several months after the onset of the disease.

More than half of the patients whose eyes are involved can be expected to lose their sight permanently in one or both eyes, and few of them can expect the return of normal function. For this reason the ophthalmologist should palpate the temporal arteries in all cases of occlusion of the retinal vessels or acute retrobulbar neuritis; conversely, he should keep in mind, when the diagnosis of temporal arteritis has been made in a patient without visual symptoms. that serious ocular trouble may supervene.

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# THE MANAGEMENT OF CHRONIC INFLAMMATION OF THE ORBITAL SOCKET\*

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Chronic and acute recurrent inflammation of the orbital socket with their attendant discharge are a source of major discomfort and inconvenience to the patient who has lost an eye. In this series of 120 such cases, bacteriologic studies were done, and the effects of various therapeutic procedures were evaluated.

# ROUTINE OF EXAMINATION

A routine of examination was evolved and carried out on each patient. First, the lid margins were examined for evidence of infection, such as blepharitis, chalazia, and hordeola. The tear sacs were palpated and expressed. Then the color and consistency of the discharge was noted. The orbital

socket itself was inspected. The presence of buried or partially exposed implants was ascertained, and the presence of skin grafts noted. The conjunctiva was examined for evidence of inflammation, and particularly for the presence of tags or crypts.

Next the patient's artificial eye was examined with the slitlamp for evidence of cracks or roughness which might cause irritation. When a defect was found, a new plastic prosthesis was ordered.

Finally smears and cultures were made of the discharge. Any material expressed from the tear sacs was left in the lower fornix. From this region the routine cultures were taken. When a blepharitis was present, cultures were also taken from the lid margins. The material collected was seeded on bloodagar and in broth. When the patient had symptoms, he was given sodium sulfacetamide (30-percent solution) four times daily

From the Department of Ophthalmology, Sunnybrook Hospital. Read at the Section of Ophthalmology, Academy of Medicine, Toronto, November, 1949.

until the culture report was received in 48 hours. At this time a drug was prescribed which would act on the organisms grown.

# PROCEDURE AND RESULTS

For the purposes of this study the cases were divided into two main clinical groups:

(1) Those with no implant or with a buried implant;

(2) those with a partially exposed integrated implant.

In Group 1 every orbit seen was included in the series, with the result that the patients' symptoms varied from those of very acute inflammation to none at all. Seventy-seven red sockets showing marked signs of inflammation were seen. Twenty-nine patients had white sockets, which were essentially asymptomatic. In many of the orbits two or more organisms were found on bacteriologic culture. An attempt has been made to separate these bacteria, with regard to their relative importance in the individual socket.

In 31 sockets, the primary invaders were mannitol-positive staphylococci. These patients usually had a moderately thick, yellowish-white, purulent discharge. Edema of the conjunctiva was a fairly constant feature. These orbits were treated with sodium sulfacetamide four times daily, and in every case the inflammation cleared satisfactorily. Repeat cultures showed no growth within approximately three weeks. The recurrence rate, however, was high, some patients having as many as three recurrences. Each time, however, they responded to sodium sulfacetamide. The presence of secondary organisms in a socket did not appear to affect the rate or degree of recovery.

In 10 orbits mannitol-negative staphylococci were thought to be the causative organisms. These sockets also were treated with sodium sulfacetamide to which they responded rapidly. In three weeks' time, no growth was obtained from any of the repeat conjunctival cultures.

In 10, the bacillus coli was grown in culture. In five of these, the organisms disappeared after treatment for one week with sodium sulfacetamide. This bacillus is undoubtedly introduced in the socket from the fingers when manipulating the prosthesis. One socket was treated with aureomycin hydrochloride. Three drops were instilled into the socket every hour while the patient was awake. This socket had previously failed to respond to sodium sulfacetamide. Cultures showed no growth at the end of six days' treatment. The discharge had disappeared and the socket was quiet and comfortable.

Four cases which failed to respond to sodium sulfacetamide were treated with streptomycin, 15 drops were inserted in the socket every hour during the day. The solution was made up to a strength of 5,000 units per cc. In each instance the socket became sterile after five days' treatment. In two of the cases there was a return of the B, coli in one month's time but the socket was quiet, there was no discharge, and the patient did not complain of any symptoms. It is felt that the B, coli reappeared as a nonpathogenic contaminant.

Of the eight cases of pneumococcus infection, three were treated topically with sodium sulfacetamide, three with penicillin, and two with aureomycin. One patient became sensitive to penicillin and therapy was changed to sodium sulfacetamide. All cases cleared satisfactorily after treatment for two weeks. Streptococcus viridans infections responded promptly to sodium sulfacetamide.

Four cases of infection with B. pyocyaneus were found. Unfortunately two of the patients did not return for treatment. Two cases are reported in full.

#### CASE REPORTS

Case 1. C. F. T., a 68-year-old white man, had an enucleation of the right eye in September, 1947, in order to radiate a carcinoma of the right ethmoid air cells. A glass-ball implant was buried in the socket. In August, 1948, the patient complained of irritation and a heavy discharge from the orbit.

Examination showed a heavy greenish discharge, and moderate conjunctival edema. Bacteriologic cultures grew B. pyocyaneus alone. Streptomycin was applied locally to the socket every hour during

the day. The streptomycin solution was made up to 5,000 units per cc. Therapy was continued for five days. Cultures at the end of two weeks were sterile, and clinically the socket was white.

Case 2. D. K., a 72-year-old white man, had his left eye enucleated in 1927 for malignant melanoma. He reported to the eye clinic in November, 1948, complaining of irritation and marked discharge from the socket. There was a heavy, yellowish-

In the other the socket improved with the original sulfacetamide therapy so this was continued. At the end of 15 days cultures showed no growth, While sodium sulfacetamide has been reported as variable in its effect on B, proteus, in this case a satisfactory result was obtained.

TABLE 1
SEVENTY-SEVEN RED SOCKETS WITH NO EXPOSED IMPLANT

Cases	Primary Invader	Secondary Organisms	Case
31	Staph. aureus aureus hem. albus mannitol pos.	Diphtheroid bacilli—C. xerosis —C. hoffmani     B. prodigiosus     Hem. influenzae	18 1 1
10	Staph. aureus aureus hem. albus	Diphtheroid bacilli—C. xerosis     —C. hoffmani     B. coli	8 2
10	B. coli	Diphtheroid bacilli Staph, aureus—mannitol neg. Nonhem. Strep.	4 2 1
8	Pneumococcus	Diphtheroids	4
3	Strep. viridans	None *	
4	B. pyocyaneus	Staph. aureus-mannitol neg. Gramneg. bacillus	2
2	B. proteus	None	
2	Strep. hem.	None	
1	H. influenzae	None	
1	B. lactis aerogenes	Diphtheroid bacilli	1
2 2 1		ococcus	

green discharge and marked edema of the conjunctiva, which was beefy-red.

Cultures grew more than 10 colonies of B. pyocyaneus. He was treated with streptomycin, 5,000 units per cc., 15 drops in the socket every hour while awake for five days. At the end of that time the pyocyaneus had disappeared but cultures showed a moderate growth of Staphylococcus aureus hemolyticus, mannitol negative. He was then treated with sodium sulfacetamide and his socket became sterile and the discharge and irritation disappeared in two weeks.

Two cases of B. proteus infection occurred. In one, the organism disappeared after 10 days of treatment with aureomycin. The streptococcal infections responded readily to either penicillin or sodium sulfacetamide treatment. No difference was found in the response to either of these drugs. One socket grew H. influenzae, this organism responded readily to aureomycin. One case of B. lactis aerogenes infection was difficult to control and is reported in full.

Case 3. J. A. H., a 25-year-old white man, had an enucleation of the left eye for gunshot wound in March, 1945. In December, 1945, he reported to the eye clinic complaining of irritation and a heavy discharge from the socket. The initial treat-

TABLE 2
TWENTY-NINE WHITE SOCKETS
WITH NO EXPOSED IMPLANT

Organisms	No. of cases
Staph. aureus aureus hem. mannitol pos. albus	3
Staph. aureus aureus liem. albus mannitol neg.	13
Diphtheroid bacilli	2
No growth	7
B. coli	3
B. pyocyaneus	1

ment consisted of swabbings with silver nitrate (one-percent solution). No cultures were recorded at that time. In January, 1946, a culture grew B. lactis aerogenes. He was then treated with penicillin ointment and the discharge showed no improvement.

At this time the glass-ball implant in the socket became dislocated, was removed, and a smaller one inserted. Following this, streptomycin therapy was initated and the orbital wound healed in two weeks. A culture at the end of that period showed a scant growth of a diphtheroid bacillus.

In the 29 white sockets (table 2) which were asymptomatic, five different organisms were grown. These were thought to be contaminants. No therapy was given.

In Group 2, the orbits with partially exposed integrated implants, only those patients who complained of irritation and discharge were studied. In this group the organisms shown in Table 3 were cultured.

The discharge from the greater number of these sockets grew mannitol-positive staphylococci on culture. These infections responded promptly to the administration of sodium sulfacetamide.

In three cases, recurrence of the staphylococcal infection was noted, but the response to the second course of sulfacetamide therapy was as prompt as to the first. Each of the three cases of B. coli infection was treated differently—one with sodium sulfacetamide, one with aureomycin hydrochloride, and one with streptomycin. Each orbit responded well and cultures became negative.

The most rapid cure, however, was observed in the socket treated with streptomycin. The streptomycin was given for five days. Cultures taken three days later were sterile.

Of the three cases of pneumococcus infection, two were treated with penicillin solution and one with sodium sulfacetamide. The sockets were sterile in two weeks. In one case treated with penicillin, pneumococci reappeared two months later. On the second occasion, sodium sulfacetamide was used. To date there has been no recurrence.

Both cases of B, pyocyaneus infection were treated with streptomycin and repeat cultures at the end of three weeks showed a scant growth of a staphylococcus. The latter organism was treated with sodium sulface-tamide and it cleared promptly. The staphylococcal infection recurred in both instances approximately 12 weeks later. Once again a satisfactory result was obtained with sodium sulfacetamide.

TABLE 3
FOURTEEN RED ORBITAL SOCKETS WITH PARTIALLY EXPOSED INTEGRATED IMPLANTS

Cases	Primary Invader	Secondary Organism	Cases
6	Staph. aureus aureus hem. mannitol positive	B. coli Diphtheroid bacilli Pneumococcus	1 1 1
3	B. coli	Diphtheroid bacilli	2
3	Pneumococcus	B. coli	1
2	B. pyocyaneus	None	

# CONTACT ALLERGY

In two orbits, contact allergy to the methyl methacrylate plastic of the implant occurred.¹ Mannitol-positive staphylococci were cultured from one socket, and B, pyocyaneus from the other. The first socket was treated with sodium sulfacetamide and the second with aureomycin. The cultures in both became sterile, but marked watery discharge, redness, and edema of the conjunctivas remained. Scrapings from the conjunctivas failed to show any eosinophiles. Surgical removal of the implants resulted in a complete cure.

Six cases of contact allergy to plastic artificial eyes occurred. These orbits presented the same symptoms as have been recorded. Patch tests in the orbital sockets with small buttons of polymerized methyl methacrylate were positive. Eosinophiles were found in the scrapings from only one case. When the plastic prostheses were removed and glass eyes substituted, the discharge and irritation ceased promptly.

The occurrence of contact allergy to plastic has been reported in the literature on numerous occasions.¹ One observer has reported that no consistent eosinophilia was found in his cases of allergy to plastic.² It was stated that basophiles in the scrapings are also an indication of allergy. This information was not available at the time the scrapings were done so that no search was made for basophiles. There are two ways of substantiating the diagnosis, one is to substitute a glass for a plastic prosthesis, the other is to use a different type of plastic. We have found the former to be the more convenient.

#### IMPROPER HYGIENE

The incidence of recurrent infection of the orbital socket is felt to be due in large measure to improper hygiene. The handling of the prosthesis with dirty hands undoubtedly is the cause of a great number of these cases. Patients have been observed to wipe the socket with used handkerchiefs, dirty

towels, and so forth. The common-sense rules of hygiene must be impressed upon the patient.

# CONJUNCTIVAL TAGS

When conjunctival tags were present, the infection did not respond until they were removed. Simple removal with cautery resulted in dramatic improvement. The tags provide deep crypts where the bacteria are not reached by antibiotics applied locally and can survive.

The three sockets in which skin grafts were found were markedly inflamed. Cultures from two showed a heavy growth of a pneumococcus and from the third a mannitol-positive staphylococcus. These sockets were kept sterile only as long as the sodium-sulfacetamide therapy was continued. When therapy was discontinued, the discharge returned, and many colonies of the organisms were again grown. Finally, the skin grafts were removed and mucous membrane grafts, taken from the lower lip, inserted. After the sockets had healed, sulfacetamide therapy was stopped. No return of the infection has occurred to date.

# USE OF STREPTOMYCIN

Streptomycin is now included in the standard armamentarium of the ophthalmologist. It inhibits the growth of B. pyocyaneus, B. coli, staphylococci, streptococci, pneumococci, and diphtheroid bacilli. Several cases of contact dermatitis have been reported. In our series it was found that the organisms became resistant to streptomycin after therapy for approximately five days. This antibiotic is particularly useful in the treatment of B. pyocyaneus infections, which respond promptly to its administration.

## USE OF AUREOMYCIN

Aureomycin hydrochloride has a wide range of usefulness. It inhibits the growth of staphylococci, streptoccci, H. influenzae, B. coli, and B. proteus, but it does not act on B. pyocyaneus. Several cases of sensitivity to this drug have been reported. The solution is made by mixing five cc. of distilled water with 25 mg. of the powder. At room temperature it remains stable for only 24 hours. There were no cases of sensitivity to this drug in our series.

# USE OF PENICILLIN

The usefulness of penicillin in cases of chronic infection is diminished by the frequent occurrence of sensitivity. This is especially marked when the ointment is used. It is, therefore, not recommend for prolonged administration.

# USE OF SODIUM SULFACETAMIDE

Sodium sulfacetamide (30-percent solution) is the most useful of all in the treatment of chronic orbital inflammation. Only one case of local sensitivity occurred, although in many patients it was administered daily for prolonged periods. It inhibits a wide range of organisms. Occasionally patients complain of a burning sensation for a few minutes after its instillation, but this is not a contraindication to its continued use.

It is incompatible with streptomycin calcium chloride, but it is compatible with streptomycin sulfate.<sup>8</sup> This fact should be remembered when both drugs are to be used in cases of mixed infection. No development of resistant strains was found.

# SUMMARY

One hundred and twenty cases of chronic inflammation of the orbital socket were investigated bacteriologically. Twenty different organisms were grown, of which staphylococci were the most common. Two cases of B. pyocyaneus and one of B. lactis aerogenes infection are reported in full.

Fourteen cases of chronic inflammation of the orbital socket in which partially exposed integrated implants had been inserted were investigated in the same manner. Mannitol-positive staphylococci were the most common infecting organism.

Eight cases of contact allergy to plastic were found. These cleared promptly on removal of the plastic prosthesis.

Sodium sulfacetamide has been found to be the most useful drug in the treatment of these conditions. Streptomycin is indicated in infections caused by B, pyocyaneus, but after local therapy for five days the organisms tend to become resistant. Aureomycin hydrochloride is particularly useful in the treatment of B, proteus and B, coli infections.

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I am indebted to Dr. J. C. Hill for permission to report his case in full. Acknowledgement is made of the assistance of Dr. Marion Ross, bacteriologist at Sunnybrook Hospital.

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# OCULAR CONDITIONS ASSOCIATED WITH IDIOPATHIC HYPERLIPEMIA\*

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The role of fat in the body metabolism has long intrigued many investigators. Ophthalmologists are aware of the variety of ocular conditions associated with lipid histiocytosis. Many of these are merely fat-storage reactions probably initiated by some local cellular irritation such as trauma, infection, or deficient oxygenation. Others such as Niemann-Pick's disease, Tay-Sachs' disease, Gaucher's disease, and the Schüller-Christian syndrome represent a systemic disturbance in intracellular fat metabolism.

It is not the purpose of this paper to describe these conditions, but rather to call attention to a rare and completely different condition known as idiopathic hyperlipemia and how the eye may be affected thereby. Before describing the picture, however, a brief review of fat metabolism is necessary.

# FAT METABOLISM

After digestion and emulsification in the small intestine, fat is absorbed into the blood stream and deposited in the fat depots. It may then be withdrawn from these depots and transported to the liver and other organs where it is metabolized.

Although certain lipids may be highly concentrated in the body cells, their concentration at the same time in the serum may be very low. An abnormal increase of lipids in the serum has been known to occur in a number of diseases. This increase may depend upon many different factors, such as the rate of absorption of fat from the intestines, its deposition in the fat depots, its mobilization from the depots in response to the demands of the tissues, and its disintegration in the various organs.

According to Thannhauser<sup>1</sup> the following lipid substances are found in normal serum:

Lipid Constituents	mg. per 100 c
Total fatty acids	200-450
Neutral fat	0-150
Total cholesterol	150-260
Free cholesterol	40-70
Cholesterol esters	105-195
Total phospholipids	150-250
Saponifiable phospholipids	
(lecithin and cephalin)	110-230
Sphingomyelin	10-30

The total fatty acid content of the serum is made up of three components: (1) The fatty acids of the phospholipids, (2) the cholesterol esters, and (3) the neutral fat. An increase in the total fatty acids may be due to a rise in either or all of these fractions.

It is important to realize that some of the serum lipids may be elevated without the others showing a corresponding rise. For instance, cholesterol and lecithin may be increased independently of the neutral fat. In such cases we should speak of "hypercholesteremia" or "hyperlecithinemia." On the other hand the neutral fat may be sharply elevated with only a moderate rise of cholesterol or lecithin. The term "hyperlipemia" is reserved for those cases in which the neutral fat is greatly increased. In such cases the serum begins to get milky when the neutral fat content rises above 500 mg. percent. A hypercholesteremia without an increase of the neutral fat never gives rise to cloudy serum.

The normal values for neutral fat in the serum vary between 0.0 and 150 mg. percent. Following a fatty meal, neutral fat usually rises after 1 to 2 hours and stays up for 3 to 6 hours, then gradually declines. Hence any chemical analyses for serum fat, to be of value, must be made during the fasting state.

In addition to this physiologic form of hyperlipemia there are two other basic types

<sup>\*</sup> From the Department of Ophthalmology, Harvard Medical School. Presented at the 85th annual meeting of the American Ophthalmological Society, Hot Springs, Virginia, June, 1949.

which have been classified by Thannhauser<sup>1</sup> as follows:

1. Transportation hyperlipemia. This is due to an increased rate of transportation of fat from the storage depots to the liver due to on overabundant mobilization of fat in response to profound chemical changes. An example of this type is diabetes mellitus. In this disease the less the sugar is being utilized the more the fat migrates to the liver. The administration of insulin makes the sugar available for combustion with the result that the fat disappears from the liver and the hyperlipemia also disappears along with the hyperglycemia. Other examples of the transportation type are:

 a. Chronic alcoholism, in which there may be damage to the liver and pancreas, with similar mechanism.

b. Starvation (in early stages only; prisoners of war undergoing prolonged starvation have not shown hyperlipemia).

c. Severe anemias and leukemias.

d. Lipid nephrosis.

e. Poisons such as phosphorus, chloroform, carbon tetrachloride, all of which damage the liver and interfere with normal metabolism.

In all these conditions the serum may have a milky or creamy appearance.

2. Retention hyperlipemia. This form of increased neutral fat in the serum is due apparently to an inadequate removal of fat from the blood stream to the fat depots and the organs that metabolize fat. It is characterized by a milky or creamy serum, less transient than that seen in the transportation type. There is a tremendous increase in the neutral fat but the phospholipids and the cholesterol may be only slightly increased. The blood sugar is usually normal but occasionally a slight glycosuria may be found. This is thought to be due to an accumulation of fat in the pancreas interfering with its function. Insulin has no effect on the level of the neutral fat as it does in diabetes. The syndrome was first described by Bürger and Grütz<sup>8</sup> in 1932 and

the descriptive name "idiopathic" was given to it by Holt<sup>a</sup> and his associates at the Johns Hopkins Hospital in 1939.

It may occur as a familial disease. The liver and spleen may be enlarged, especially in children, and attacks of high abdominal pain are not infrequent. If the cholesterol level is also high, there may be secondary xanthomatosis consisting of yellowish papular eruptions on the buttocks, extensor surfaces of the extremities, face, eyelids, fingers, toes, and hard palate. Otherwise the patients are perfectly well and the creamy serum is discovered accidentally.

The cause of idiopathic hyperlipemia is unknown. The literature contains only one report of autopsy findings. In this patient, a one-year-old child, no cause for death was found. The liver and spleen were enlarged, and many fat-containing cells were present in the spleen, bone marrow, and lymph nodes. No foam cells were found in the liver and chemical analysis of this organ showed no increase of lipids above normal.

# OCULAR MANIFESTATIONS

Apparently the eyes may be affected in three ways: (1) The fundus may show the picture of lipemia retinalis, (2) the cornea may show a lipid keratitis, (3) the eyelids may show eruptive xanthomatosis, quite different from the ordinary flat xanthelasma commonly seen.

# LIPEMIA RETINALIS.

This is seen occasionally in diabetes. Since Heyl<sup>5</sup> reported the first case in 1880, some 65 other instances have appeared in the literature. It may also occur without diabetes in cases in which the neutral fat in the serum reaches about 2,000 mg. percent.

Although it has long been known that the serum lipids may be increased in other diseases, it was believed until fairly recently that only in diabetes was lipemia retinalis seen and that its presence was indicative of acidosis. We now know that this is not necessarily so, as visible fat in the retinal

vessels is simply an indication of an excessive amount of neutral fat in the serum from whatever cause. Most authors say that, if the total fat content reaches four percent, the fundus will present the picture of lipemia retinalis, but this is not strictly true, for by this figure they usually refer to the total fatty acids present. But it is the neutral fat fraction which is the important one. The total cholesterol may be very high but unless the neutral fat is also high there will be no lipemia retinalis.

Only eight nondiabetic cases of lipemia retinalis have been reported in the literature, one by Wagener<sup>6</sup> in 1922, two by Holt<sup>3</sup> in 1939, one by Bernstein<sup>7</sup> in 1939, one by Goodman<sup>6</sup> in 1940, one by Kauffman<sup>9</sup> in 1943, one by Lepard<sup>10</sup> in 1944, and one by Grossmann and Hitz<sup>11</sup> in 1948.

In Wagener's case the patient, a nine-yearold boy, had received extensive radiation therapy for lymphatic leukemia and it was thought that this had resulted in enough tissue destruction to cause the high fat values in the serum.

In Kauffman's case, the patient was an alcoholic and therefore probably had some pancreatic or liver damage which resulted in increased fat in the blood.

This leaves only six cases of lipemia retinalis which can be truly ascribed to "idiopathic hyperlipemia" in that they occurred in otherwise well people who were capable of metabolizing fat and in whom no metabolic cause could be found for the condition. The following case is, I believe, the seventh to be reported.

## CASE REPORT

Mr. S. R., a 47-year-old insurance salesman, consulted Dr. Siegfried Thannhauser in January, 1946, because of a yellowish itchy eruption on his body. The eruption had been recurring for almost a year and had involved chiefly the extensor surfaces of his arms and legs. Aside from this he felt perfectly well.

Past history. He had always been in good

health but was inclined to be somewhat obese.

Family history. Irrelevant; no history of diabetes, tuberculosis, or disturbance of fat metabolism.

Physical examination. The patient appeared to be a well-nourished middle-aged male in good health. Weight, 203 pounds. There was a pruritic eruption on his elbows, wrists, knees, and shoulders, consisting of fine, yellow-red nodules arising from a thin, reddish base.

The heart and lungs were normal; blood pressure was 140/90 mm. Hg; no enlargement of liver or spleen; X-ray studies of chest were normal; right diaphragm seemed rather high on fluoroscopy. Red count, 5.15 million; white count, 7,500; hemoglobin, 19.1 gm.; urine, clear, acid, specific gravity 1,035; albumin 0, sugar "yellow," sediment showed rare W.B.C., fasting blood sugar, 206 mg. percent, Hinton negative.

Ocular examination. Externally the eyes were perfectly normal. Vision 20/20 in each, Ocular tension was normal to palpation. Slit-lamp examination revealed no changes in the cornea or lens of either eye. Peripheral and central fields were normal. Both fundi showed the typical picture of lipemia retinalis. The arteries and veins were almost indistinguishable from one another, appearing as broad cream-colored ribbons against a milky background.

The serum was creamy and opaque, Analysis on January 16, 1946, showed the following:

Lipid Constituents in mg. % No	rmal Values
Total fatty acids5,196	200-450
Neutral fat	0-150
Total cholesterol 693	150-260
Free cholesterol 325	40-70
Cholesterol esters 369	105-195
Total phospholipids 810	150-250

It will be seen that there is an enormous increase in the neutral fat, with the cholesterol and phospholipids being high also.

A diagnosis of idiopathic hyperlipemia was made and the patient put on a diet of 1,600 calories consisting of carbohydrate, 170 gm.; protein, 185 gm.; and fat, 20 gm. The hyperglycemia was not considered to be a true diabetes and no insulin was given.

The lipemia retinalis disappeared in a few days on this regime. One month later marked regression of the skin lesions was apparent. He had lost 15 pounds and felt fine. The fundi were normal. The fasting blood sugar was 130 mg. percent. The serum was no longer creamy and chemical analysis on March 27, 1946, showed the following:

Lipid Constituents in mg. % No.	rmal Values
Total fatty acids688	200-450
Neutral fat	0-150
Total cholesterol292	150-260
Free cholesterol 76	40-70
Cholesterol esters216	105-195
Total phospholipids195	150-250

The patient adhered fairly strictly to his diet for a year but then began to eat heavily again. In May, 1947, the lipemia retinalis had returned but there was little evidence of secondary xanthomatosis. The fasting blood sugar was 131 mg. percent. Chemical analysis of his serum on May 16, 1947, revealed the following:

Lipid Constituents in mg. %	Vormal Values
Total fatty acids3,100	200-450
Neutral fat2,525	0-150
Total cholesterol 375	150-260
Free cholesterol 150	
Cholesterol esters 225	
Total phospholipids 350	150-250

The patient returned to his diet and the lipemia retinalis disappeared in a few days as the neutral fat level dropped down to 1,688 mg. percent.

He remained on his diet fairly well for the next year and a half and then the cutaneous lesions began to reappear. Examination of the fundi showed definite lipemia retinalis and chemical analysis of his blood on December 3, 1948, showed the neutral fat and cholesterol sharply elevated.

Lipid Constituents in mg. % No.	Normal Value:	
Total fatty acids4,155	200-450	
Neutral fat3,497	0-150	
Total cholesterol 753	150-260	
Free cholesterol 317	40-70	
Cholesterol esters 436	105-195	
Total phospholipids 530	150-250	

Comment. In this patient the lipemia retinalis paralleled the neutral fat level of the serum. It was impossible to get blood samples at the exact time the lipemia retinalis appeared and disappeared as the patient was an active businessman feeling perfectly well and he refused to be hospitalized for observation. However, as far as could be told, the retinal vessels always appeared normal when the neutral fat dropped below 2,000 mg. percent and were found to be milky or creamy when it rose to 2,500 mg. percent or above.

The figure of 500 mg, percent is the one usually given at which milkiness of serum becomes evident but this refers to centrifugalized serum with blood cells removed. This is an entirely different situation from circulating blood in the retinal vessels where a much higher level of neutral fat is necessary for lipemia retinalis to make itself manifest.

The cutaneous lesions occurred only when the cholesterol level was markedly elevated. They disappeared when the cholesterol approached normal values, even though the neutral fat level remained high. This particular type of xanthomatosis appears to be dependent upon a hypercholesteremia in conjunction with a high neutral fat level.

The cornea was absolutely normal, no evidence of even an arcus senilis being seen.

# XANTHOMAS OF EYELIDS

The ones seen in idiopathic hyperlipemia are quite different from the ordinary xanthelasma familiar to all ophthalmologists. They are small yellow plaques arising from an inflammatory base, and are associated with similar cutaneous xanthomatous lesions elsewhere. They are identical to the type seen in some diabetics.

They are associated not only with a high neutral fat serum level but also with a hypercholesteremia, whereas the common type of xanthelasma, although associated in many cases with an increased serum cholesterol, is probably due primarily to a local degenerative change in the skin. Montgomery<sup>12</sup> points out that, although many foam cells occur in xanthelasma, there is rarely a foam cell found in the eruptive type of xanthoma.

There has been considerable confusion as to xanthomatous disorders. Thannhauser and Magendantz13 believe they may be classified according to the laboratory findings in the serum, in the following manner:

1. Essential xanthomatosis of the hypercholesteremic type. Increased serum cholesterol, moderately increased lecithin, normal neutral fat. (This blood picture may be associated with tuberous or plain xanthomas of the skin, xanthomas of the tendons, atheroma of the intima of the blood vessels and endocardium of the heart, and in lining of bile ducts.)

2. Normocholesteremic xanthomatosis. Normal values for cholesterol, lecithin, and neutral fat. (This picture is found in eosinophilic granuloma, Schüller-Christian syndrome, and eosinophilic xanthomatous granuloma. Disseminated xanthoma of the skin may occur along with involvement of the osseous system, dura, brain, lungs, lymph nodes, and spleen.)

3. Hyperlipemia with secondary xanthomatosis. Extremely high level of neutral fat with moderately increased cholesterol and lecithin, (This is seen in diabetes and idiopathic hyperlipemia. The xanthomas here are eruptive and rise from a thin inflammatory base.)

#### LIPID INTERSTITIAL KERATITIS

Another ocular condition which may be associated with idiopathic hyperlipemia is lipid interstitial keratitis. The following case is, as far as I know, the only instance of it that has been reported in this disease.

# CASE REPORT

Mr. V. J., aged 41 years, a hotel manager, came to the hospital on June 12, 1947, complaining of irritation of the left eye of three weeks' duration. There was no history of trauma. He had consulted a doctor who told him he had an ulcer of the cornea and prescribed atropine and penicillin ointment without relief.

Past history. The patient had always been well. There had been a recurring yellowish infiltration on the top of his nose for the past two years. Also he often had attacks of pain in the left heel with no external signs of inflammation. Three years ago, while serving in the army overseas, he had a similar attack of irritation in the right eye which lasted several weeks and finally subsided with boricacid instillation with practically no impairment of vision,

Family history. Irrelevant. No diabetes, tuberculosis, or disturbances of fat metabolism.

Ocular examination. The conjunctiva of the left eye were slightly congested and there was slight photophobia, The visual acuity was 20/30. The cornea showed a deep solidlooking opacity extending from the 12o'clock position around nasally to the 4o'clock position, leaving a small, clear area centrally and a small, clear area in the upper temporal quadrant. There was no staining with fluorescein. The opacity had a faintly yellowish tinge.

Slitlamp examination showed the opacity to consist of wedges of closely packed granules arranged in radiating bands from the periphery toward the center but not infringing on the central part of the cornea. There was a narrow, relatively clear zone at the limbus. Only the stroma appeared involved, the epithelium being intact. No vascularization was apparent at this first examination. There was no evidence of uveal inflammation.

The right eye, which had been involved three years previously, showed a somewhat similar picture. There were no signs of congestion or irritation, and the visual acuity was 20/30. The opacity involved the stroma nasally and below from the 3- to 9-o'clock positions, leaving a large, clear area centrally and above.

Slitlamp examination showed intact epi-

thelium but infiltration of the anterior part of the stroma with the same wedges of closely packed granules and in addition a pattern of lacy criss-cross lines made up of highly refractile dots in the posterior part of the stroma. These were thought to be cholesterin crystals. There were a few old deep and superficial vessels at the limbus crossing a clear zone of the cornea which existed peripheral to the opacity. There was no sign of old uveal inflammation.

In both eyes the ocular tension was not elevated and ophthalmoscopic examination revealed perfectly normal fundi.

A diagnosis of lipid interstitial keratitis was made and the patient was sent to Dr. Siegfried Thannhauser for general physical examination and blood chemistry studies.

General physical examination. Aside from the blood findings this was essentially negative. No xanthomatosis was present. Heart and lungs were normal; blood pressure, 140/90 mm. Hg; fluoroscopy of chest, normal; liver and spleen not enlarged; urine amber, acid reaction, specific gravity 1,020, albumin 0, sugar 0, sediment occasional mucous thread and occasional white cell; fasting blood sugar, 100 mg. percent; Hinton negative, serum uric acid 4.5 mg. percent.

The blood serum was creamy. Fasting analysis for serum lipids on June 16, 1947, gave the following results:

Serum lipids in mg. % No	rmal Value.
Total fatty acids1,360	200-450
	0-150
Total cholesterol 292	150-260
Free cholesterol 122	40-70
Cholesterol esters 170	105-195
Total phospholipids 328	150-250

It will be seen that whereas the total fatty acids are definitely increased this is due to a tremendous rise in the neutral fat fraction, the cholesterol and the phospholipids being only slighly elevated. In the absence of diabetes or any disturbance of liver function, a diagnosis of idiopathic hyperlipemia was made but, since the left eye was beginning to show signs of improvement under simple treatment of hot packs and atropine instilla-

tions, no reduction in fats was recommended in his diet in order to see what the blood would show after the eye had cleared.

In two weeks the left eye had shown marked improvement and all signs of irritation had ceased. Slitlamp examination showed a definite fading of the corneal infiltration from the center outward. There were now a few superficial and deep blood vessels invading the cornea below and nasally. Also a lacy pattern of criss-cross lines deep in the stroma was becoming evident.

A fasting sample of blood was taken for analysis on July 2, 1947, and to our surprise showed the following:

Serum lipids in mg. %	No	rmal Values
Total fatty acids2	,190	200-450
Neutral fat		
Total cholesterol	262	150-260
Free cholesterol	125	40- 70
Cholesterol esters	137	105-195
Total phospholipids	375	150-250

In spite of the fact that the eye was well on its way to recovery the total fatty acids and neutral fat in the serum were much greater than on the first analysis two weeks previously. However, the patient was now put on a diet of 1,600 calories daily containing only 50 gm. of fat. In addition he was given one gm. of thyroid daily even though his serum cholesterol was not elevated.

During the next five months he continued his diet and there was no further trouble with the eye. The corneal opacity continued to decrease. An analysis of his blood serum on December 1, 1947, showed the following:

Serum lipids in mg. % No.	rmal Values
Total fatty acids924	200-450
Neutral fat	0-150
Total cholesterol204	150-260
Free cholesterol100	40- 70
Cholesterol esters104	105-195
Total phospholipids252	150-250

Two months after this analysis the patient had a recurrence of his keratitis in the right eye which had been quiescent for four years. Examination revealed the presence of two superficial infiltrates at the nasal limbus with some superficial vascularization. There was no staining with fluorescein. Cultures were negative.

Slitlamp examination showed an increase of the stromal opacity, chiefly nasally infringing toward the center. There was no sign of uveitis. In a week the condition had subsided under hot boric soaks and no other local treatment.

A serum analysis on February 12, 1948, showed the following results:

Serum lipids in mg. %	No	rmal Value
Total fatty acids	,125	200-450
Neutral fat	953	0-150
Total cholesterol	260	150-260
Free cholesterol	94	40- 70
Cholesterol esters	166	105-195
Total phospholipids	280	150-250

To date he has no further trouble in spite of the fact that he has not adhered to his low-diet and as a result his last serum analysis, on December 22, 1948, showed the neutral fat at high level:

Serum lipids in mg. % No	rmal Values
Total fatty ac'ds	200-450
Neutral fat	0-150
Total cholesterol 250	150-260
Free cholesterol 77	40-70
Cholesterol esters 173	105-195
Total phospholipids 210	150-250

#### DISCUSSION

An analysis of the case presented last shows there is no correlation between the fat content of the serum and the severity of the keratitis. Also it should be noted that the corneal lesion appears to be identical, clinically, with some cases of primary lipid interstitial keratitis in which the serum levels for fat have been found to be perfectly normal. This fact raises the question as to whether or not the keratitis here was merely a coincidence. However, when we realize that both idiopathic hyperlipemia and primary lipid interstitial keratitis are very rare conditions, and that both represent a disturbance in fat metabolism, it seems fair to assume that some relationship exists between them, especially when they occur simultaneously in one individual.

The question arises as to how the fat gets

into the cornea. Is it brought there by the blood or is it synthesized within the cell? The literature contains much speculation on this subject. Heath<sup>14</sup> feels that, in both primary lipid keratitis and those lipid keratitis cases secondary to trauma or infection, the essential process is the same and the material comes from without, a local activating lesion being necessary to initiate the lipid cellular response. He believes that the normally fine fat emulsion is precipitated or coarsened and that this produces the foreign-body type of reaction.

Katz and Delaney<sup>10</sup> are of the opinion that the fat in the cornea may be brought there by the blood and may also be liberated by the cell itself whenever oxidation is interfered with

Waldever16 and Thannhauser1 both feel that the reticulum cells and histiocytes may retain functional possibilities of embryonal cells and thus they may be able to form lipids including cholesterol, Thannhauser1 conceives it possible that a disturbance of the intracellular enzymes results in an accumulation of cholesterol within the cells, transforming them into foam cells. This is contrary to the general belief that the foam cells are phagocytic cells which wander into the cornea in order to ingest and store unwanted material. The fact that macrophages are not found in normal corneas but accumulate during an attack seems to substantiate this generally accepted view.

Another possibility is that the presence of hyperlipemia calls forth the macrophages of the reticulo-endothelial system which ingest fat either in the blood stream or in some tissue remote from the eye. Then, in response to some mild activating lesion, these fat-laden cells invade the cornea.

But whether the fat is brought to the cornea by the blood or synthesized within the cell there must be either some primary defect of cell metabolism or some disturbance of limbal circulation. The exact mechanism is not known.

Heath14 has suggested several possible

contributing factors such as lowered temperature of the avascular cornea, exposure to repeated mild trauma, and toxins from local and distant sources of infection.

Cogan<sup>17</sup> assumes that the fat and the constituents which keep it in solution in the blood have different rates of loss from the corneal stroma. As the dissolving constituents are selectively abstracted from the cornea by the surface membranes, the fat comes out of solution and is deposited in the corneal stroma, forming an arcus senilis or a lipoid infiltration, depending on the previous state of corneal vascularization and the degree of lipemia.

## CONCLUSIONS

Idiopathic hyperlipemia is a rare clinical entity of unknown etiology characterized by an enormus increase of neutral fat in the serum. It may occur in individuals who are capable of metabolizing fat and who have no disturbance of sugar metabolism.

The associated ocular abnormalities are lipemia retinalis and lipid interstitial keratitis, a case of each being reported here. Secondary xanthomatosis, sometimes involving the eyelids, may occur if a hypercholesteremia accompanies the rise in the neutral fat.

The lipemia retinalis and the xanthomatosis can be made to disappear by drastically reducing the fat in the diet. The exact mechanism producing the lipid interstitial keratitis is difficult to explain. Several theories have been suggested but to date none has been proved.

243 Charles Street (14).

The chemical analyses for blood lipids in these cases were done by Dr. S. J. Thannhauser at the Pratt Diagnostic Hospital, Boston, Massachusetts.

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#### OPHTHALMIC MINIATURE

The eye may be said to resemble a microcosm, in which may be discovered all the various morbid changes which take place throughout the other organs and tissues of the body.

A Treatise on the Diseases of the Eye, George Frick, Baltimore, 1823.

# THE CRISP-STINE TEST FOR ASTIGMATISM AND THE LEBENSOHN ASTIGMOMETER

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The publishing of two closely related papers ("A simplified astigmometer," by Lebensohn,1 and "A further, very delicate test for astigmatic axis, using the cross cylinder with an astigmatic dial and without the use of letter chart," by Crisp and Stine<sup>3</sup>) in the same issue of the JOURNAL was a fortunate and fine piece of editing; Lebensohn has made an excellent contribution to the clearer understanding of the use of astigmatic dials in general, and in the Crisp-Stine test in particular. It is gratifying that further interest and research has been aroused in a subject already rather exhaustively investigated. Precision and practical accuracy in refraction should be the goal of every ophthalmologist.

As I stated in closing the discussion of our paper before the Section on Ophthalmology of the American Medical Association in 1948. I had computed the effects of obliquely crossed cylinders in the Crisp-Stine test, tabulating many examples. This mathematical analysis explained and confirmed our clinical experience with the test, but it was not, for the sake of brevity and simplicity, included in the original presentation. In this supplemental paper, I propose to discuss further the optics and clinical aspects of the rotating cross-line dial test for astigmatic axis, used both with and without the cross cylinder, and Lebensohn's modification thereof.

The addition by Lebensohn of the arrowhead lines to the rotating single cross-line dial is ingenious, but I have not found that the test is thereby simplified, especially for the patient. A multitude of lines on astigmatic dials is often confusing, a consideration which led to Lancaster's advocacy of the two-meridian rotating cross, rather than the wagon-wheel type of dial, for the more accurate determination of the amount of

astigmatism, and to its adaptation for the determination of the axis by Dr. Crisp and me.

The lines of the rotating cross are 90 degrees apart and, as Lebensohn points out, to place them exactly astride the axis of the trial cylinder requires the mental arithmetic of subtracting or adding 45 degrees to the position of the trial cylinder axis. However, this simple computation is rendered unnecessary by marking a small triangle or line on the periphery of the rotating dial exactly halfway between the two cross lines to designate the position of the axis of the trial cylinder, as shown in our original illustrations.

If one wishes, however, to add the arrowhead lines to the rotating cross, for maximum sensitivity the angle between the arms of the inverted V should be 90 degrees, not 60 degrees as advocated by Lebensohn and Verhoeff. A little calculation with the equations for obliquely crossed cylinders and the power of cylinders in a given meridian will show why this is so.

Consider, for example, an error of simple hyperopic astigmatism of 1.0D., axis 90 degrees (-1.0D. cyl. ax. 90°) requiring correction with +1.0D, cyl. ax. 90°. If this trial cylinder, of correct strength, is erroneously placed as little as one degree off-axis, for example, at axis 89 degrees, there is produced a new, or "secondary" (Linksz³) mixed astigmatic error, -0.017 +0.034 cylinder axis 44.5°, which is 44.5 degrees away from the axis of the trial cylinder (89 degrees).\*

<sup>\*</sup> This striking phenomenon can be demonstrated and studied on the optical bench; also by the superposition of two trial-case cylinders of the same power but opposite sign (one, the "eye error" cylinder and the other, the correcting lens) at different axes, and measurement of the resultant axis on a protractor; by viewing the image of a wagon-

If the lines of the relating cross or the arms of the arrowhead, the angle between which is 90 degrees, are placed exactly astride the axis of the trial cylinder, they will coincide almost exactly—within one-half degree—with the meridians of greatest and least refraction of the row astigmatic error, and the astigmatic difference or contrast between the lines will be reaximum.

One might consider also an example of even greater displacement of the axis of the plus 1.0D. trial cylindes, say to 70 degrees, or 20 degrees from the correct axis. In this case, the resultant "secondary" error is -0.34 + 0.68 axis  $35^{\circ}$  (correctible by +0.34 - 0.68 axis 35°, 4r - 0.34 + 0.68 axis 125°). The lines of the rotating cross placed exactly astride the axis of the trial cylinder will be at 25 and 115 degrees, and the difference between the dioperic powers of the cylinder in these meridians-0.02D., in the former and 0.66D., in the latter-is 0.64D. The wings of Lebensohn's arrowhead will be in the 40 and 100 degree meridians, the astigmatic difference between which is but 0.55D.

Other examples, including those of overand undercorrecting trial cylinders at several other erroneous axes, have been computed with the same end-result. For maximum sensitivity, the arms of the arrowhead or inverted V should form an angle of 90 degrees with each other, or 45 degrees with either side of the arrowshaft one which designates the axis of the trial cylinder.

wheel dial on the ground-hass plate of a camera in front of which is held similar combinations of cylindric lenses, or by phitography under these conditions; by cylinder reinoscopy; and subjectively by the refractionist himself.

With such a small deviation of trial cylinder axis, one will discern the effect more easily and conclusively by the use of cylinders of greater power, say plus and minud 10 diopters or more. The power of the trial cylinder, provided it is of the correct strength, will not affect the position of the axis of the new error as given above, but will, of course, result in a greater or lesser astigmatic error in direct proportion no the strength of the cylinders, that is, with 1017 cylinders the resultant error will be 10 times as freat, -0.17 +0.34 axis 44.5°.

The sensitivity of the rotating single cross dial, under the proper conditions of fogging and lighting of the charts, is 0.03D., of astigmatic difference. Regan<sup>4</sup> has repeatedly and consistently demonstrated such exquisite discrimination clinically, using a plus 0.03D, cylinder in testing for strength once the correct axis of the trial cylinder has been located.

In the test for axis, this is equivalent to a displacement of the axis of a 1.0D. cylinder, one degree (see above), or to a five-degree shift in the axis of a 0.25D. cylinder. That is to say, the improper position of a correct 0.25D. cylinder five degrees from the true axis produces the error of -0.02 + 0.04 cylinder at an axis 42.5 degrees from the axis of the trial cylinder, and an astigmatic difference of 0.04D., between the dial crosslines placed exactly astraddle the axis of the trial cylinder.

Many patients are able to discern this small degree of contrast although they may report merely that one cross line is slightly doubled, rather than that one of the lines is actually sharper than the other. The addition of the 0.12D, cross cylinder in the Crisp-Stine procedure will aid the patient's discrimination and verify the findings.

With such a small cylindric error it is true that in neither position of the cross cylinder will the dial lines appear perfectly uniform—the astigmatic difference between the two lines is 0.29D., in one position, and 0.20D., in the alternate—but the net change produced by the "flip" of the cross cylinder is 0.09D., which is slightly more than double the degree of contrast produced by erroneous position of the axis of the trial cylinder alone (0.04D.).

In the first instance, that is, without the use of the cross cylinder, the refractionist will turn the plus trial cylinder away from the blurred cross line toward the sharper one, until the effect is reversed, or the two lines appear equal in intensity. In the Crisp-Stine test the plus trial cylinder is turned toward the plus axis of the cross cylinder in the position in which the two cross lines appear



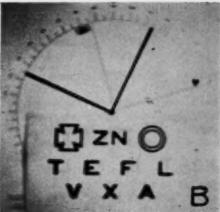


Fig. 1 (Stine). Basic error of camera lens, rendered ametropic, requires a final need for correction with -0.25D. sph.+1.0D. cyl. ax. 60°. In (A) and (B) the correcting +1.0D. cylinder had been inaccurately placed at axis 70 degrees. The two lines of the rotating cross were set respectively at 25 and 115 degrees. The 0.12D., cross cylinder was first (A) placed with its plus axis at 115 degrees, and then (B) with its plus axis at 25 degrees. The choice as to relative uniformity of the two lines is obviously for the second of the two positions, indicating that the correcting plus cylinder should be turned toward 60 degrees. The astigmatic difference between the two lines is 0.59D., in (A) and 0.09D. in (B).

relatively uniform, and the end-point is reached when the variation of emphasis, or the reversal of sharpness from one dial line to the other, is equal in both positions of the cross cylinder.

The optical effects and technique of the Crisp-Stine test are clearly illustrated by the photographs published with our original paper. An additional illustration is afforded by the excellent photographs given me by Dr. John Matthews of San Antonio, Texas.

In Figure 1 the correcting +1.0D, cylinder is 10 degrees off-axis at 70 degrees, the proper axis being 60 degrees. The resultant secondary error is -0.17 +0.35 cylinder axis 110°, and the astigmatic difference between the two lines of the rotating dial placed astride the axis of the trial cylinder in the 25- and 115-degree meridians is 0.34D.

The patient, slightly fogged, should report that the 25-degree (10 o'clock) line is sharper than the 115- (one o'clock) degree line, and thus indicate that the trial cylinder should be turned toward the sharper dial line, that is toward 60 degrees.

The addition of the 0.12D, cross cylinder with its plus axis at 115 degrees (-0.12

+0.25 axis 115°) produces the tertiary error of -0.29 +0.59 axis 112.1°, and an enhanced astigmatic difference of 0.59D., between the two cross lines, the 25-degree cross line being still the sharper line (fig. 1-A). (A similar degree of contrast would be produced by a correcting +2.0D. cylinder offaxis at 68.4 degrees without the use of the cross cylinder.)

When the plus axis of the cross cylinder is twirled to the opposite meridian of 25 degrees, the resultant error is -0.05 +0.11 axis 98.2°, and the astigmatic difference between the cross lines is only 0.09D. The cross lines will obviously appear more uniform with the cross cylinder in the latter position (fig. 1-B).

If one were using minus cylinders in this example, the minus trial cylinder would be at axis 160 degrees, but the optical effects and procedure would be the same. The axis of the minus cylinder should be turned away from the sharper dial line toward the blurred one; and in using the cross cylinder the minus axis of the trial cylinder should be rotated toward the minus axis of the cross cylinder in the position that makes the cross



Fig. 2 (Stine). This photograph illustrates perfect correction of the error. The addition of test letters and so forth was for the purpose of comparative studies.

lines appear more uniform.

Thus we see that the cross cylinder enhances the astigmatic difference or contrast between the two dial lines when applied in one position, and reduces or neutralizes it in the alternate position, and the change is abrupt and of a degree readily detectable by the patient.

Analysis of a large number of combinations shows that the net change of contrast, derived by subtracting the astigmatic differences produced by the alternate positions of the cross cylinder, can be almost double that obtained by "rocking" the trial cylinder alone. And this ratio of two to one is maintained throughout the range of weaker astigmatic errors up to 1.5D., and errors in placement of the axis up to 15 degrees, regardless of whether the trial cylinder is too weak, too strong, or of correct strength.

In the larger astigmatic errors, the use of the cross cylinder may offer little advantage over the simple turning of the trial cylinder, unless the error in axis is five degrees or less. Then for the final precise determination we resort to the cross cylinder, using the 0.12D., or only occasionally the 0.25D., depending on the needs of the case.

By way of recapitulation we may postulate two mnemonic aids in testing for astigmatic axis with the rotating single cross dial. First, in the test without the cross cylinder, we utilize the principle, derived from common observation in fogging technique, that plus blurs and minus clears. The plus trial cylinder, if at the wrong axis, will produce contrast between the straddling dial lines and should be turned toward the blacker, sharper cross line (which will blur it); and similarly, the minus trial cylinder should be rotated toward the blurred line (which will clear it).

Secondly, using the cross cylinder as in the Crisp-Stine procedure, the trial cylinder is to be turned toward the axis of the cross cylinder of like sign in the position which renders the dial lines more uniform. The dictum is, plus toward plus, minus toward minus

Finally, the ideal of reversal from pronounced contrast to absolute uniformity of the dial lines is not attainable, except in rare instances, with any type of astigmatic dial, but one comes closer to it with the rotating right-angle cross, as demonstrated by experiment, mathematical analysis, and clinical experience. The Lancaster-Regan rotating cross is a highly sensitive and extremely simple test-object and, owing to the optics of obliquely crossed cylinders, is admirably suited for the precise determination of the axis as well as the strength of the cylindric correction, especially when used in conjunction with Jackson's cross cylinder in the Crisp-Stine test.

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# MASSIVE INTRAOCULAR HEMORRHAGE FOLLOWING SEVERE CEREBRAL VASCULAR ACCIDENT\*

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Although the occurrence of intraocular hemorrhage associated with subarachnoid hemorrhage is not rare, 8, 5, 9, 10 its occurrence in cerebral hemorrhage unassociated with blood in the spinal fluid is of sufficient interest to report. The ocular and neurologic findings were considered quite unusual. The course and manner of occurrence of the intraocular hemorrhage in this case presents an interesting speculative problem.

According to Riddoch and Goulden,<sup>12</sup> there are three main groups in the etiologic classification of subarachnoid hemorrhages: (1) Traumatic rupture of meningeal vessels, (2) primary intracerebral hemorrhage, the blood reaching the subarachnoid space by bursting through the brain substance, and (3) nontraumatic rupture of a meningeal vessel or basal aneurysm. Most cases are in the third classification.

In many instances, the actual rupture of the aneurysm is preceded by slow leaks producing sudden severe headaches and tinnitus. Such attacks may recur many times, eventually to be followed by a large rupture productive of coma, signs of meningeal irritation and cerebral compression, and finally death.

Less severe leaks of blood may produce an initial period of coma, followed by meningeal irritation with delirium, restlessness and vomiting, severe headache, nuchal rigidity with positive Kernig's sign, evidence of pyramidal tract disturbances, and so forth. Recovery from such an attack is not uncom-

mon but generally the attacks recur and may prove fatal.<sup>6</sup>

Although not present in all cases of subarachnoid hemorrhage, ocular signs occur with sufficient frequency to be of significance. Retinal hemorrhages and papilledema are the most common ocular findings.

The hemorrhages may occur within, in front of, or behind the retina, and may rupture into the vitreous. 10 They may be large or small, may be situated near the disc or far removed from it. According to Manschot, 10 the large profuse hemorrhages situated in the neighborhood of the disc are almost pathognomonic of subarachnoid hemorrhage and are easily distinguishable from those due to thrombosis of the central retinal vein, papilledema, retinitis, and branch occlusion of the central retinal vein.

Papilledema is often of moderate degree, occurring in about one sixth of the cases.<sup>10</sup> It may be of rapid onset or may not appear for months.<sup>11</sup>

Cranial nerve palsies likewise are common. The third and sixth nerves are usually involved. Proptosis and disturbances of conjugate gaze are also occasionally seen. Loss of vision may be complained of when the patient recovers consciousness. In the presence of these findings, the diagnosis of subarachnoid hemorrhage may be confirmed by finding blood in the spinal fluid.

The origin of the blood in the retina and optic-nerve sheaths has aroused considerable controversy and many theories have been advanced to account for it. The oldest theory is that the blood spreads from the intracranial subarachnoid space through the optic foramen into the perineural subarachnoid space and from there into the eye, either by penetrating the nerve at the lamina cribrosa or by penetrating the sclera at the anterior end of the intervaginal space. <sup>10</sup> Paton<sup>11</sup> believes

<sup>\*</sup>From the Department of Ophthalmology, Birmingham Veterans Administration Hospital, Van Nuys, California. Sponsored by the Veterans Administration and published with the approval of the chief medical director. The statements and conclusions published by the author are a result of his own study and do not necessarily reflect the opinion or policy of the Veterans Administration.

that, in a small percentage of cases, this is the route taken, the blood leaking from the sheath through the lymphatic spaces at the sides of the lamina cribrosa and along the central vessels into the nervehead and eye. This view, however, has failed to obtain histologic proof.

Various authors<sup>6,9,10,12</sup> have reported cases studied pathologically in which there was no continuity between the hemorrhage about the nerve and that within the eye. Also pathologic studies have proved the pia and optic nerve to be free of blood while the dura and sheaths of the central vessels have shown blood.

Another factor against this theory is the frequent occurrence of intraocular hemorrhage associated with hemorrhage into the pons and other intracranial structures without the presence of subarachnoid hemorrhage.

It is now generally agreed by most<sup>9,10,13</sup> that the cause of the intraocular hemorrhage is essentially the same as that causing papilledema, that is, the increased intracranial contents; there is not only occlusion of the central retinal vein by the blood distended nerve sheaths producing venous stasis but, in addition, the venous blood in the nerve is acutely pressed back into the retinal veins by the high arterial pressure in the intervaginal space. The retinal veins are unable to withstand this pressure from both directions and consequently rupture.

The frequent large intraocular hemorrhages seen in this condition, in contrast to the smaller ones seen in occlusion of the central retinal vein, are due to the sudden onset of the occlusion. As the nerve sheaths become more and more distended, the vein becomes more and more angulated, the obstruction becomes aggravated, and finally a rupture occurs at the weakest point in the vein, generally where it is crossed by an artery.

Because of the fact, however, that hemorrhages are not always limited to the area drained by the central retinal vein but occur also in the orbital and ocular tissues—dural

sheath, about the vessels of the circle of Zinn, on the episclera, in the orbital fat and muscles, and in the fibrous sheaths surrounding the ciliary ganglion and posterior ciliary nerves-Ballantyne<sup>2</sup> believes that the sudden rise in intracranial pressure, caused by the massive intracranial bleeding, compresses the veins and sinuses which receive blood from the eye and orbital structures and thus produces the stasis necessary for the occurrence of hemorrhages. He suggests further that some of the signs associated with subarachnoid hemorrhage, such as pareses of the extraocular muscles and disturbances of conjugate movements, may be due to hemorrhages in the midbrain similar to those found elsewhere.

The following case is reported because of its unusual ophthalmoscopic findings and because of the similarity of the fundus lesions to those described as characteristic of subarachnoid hemorrhage; however, in this case no blood was ever found in the spinal fluid.

## CASE REPORT

A. A. R., a 40-year-old white man of Italian descent, was admitted to the hospital on January 5, 1947, in coma with vomiting and paralysis of the right side of his body.

According to his wife, on the night of admission to the hospital, the patient went to bed at 10 P.M. About five minutes later he screamed aloud, rose up in bed, and immediately fell back in coma in which he remained for three weeks. His wife noticed at this time that his left eye was markedly proptosed. Prior to this, the patient had been in good health with no visual disturbances or hypertension. He had had infrequent headaches for the past two years but this was attributed to a blow on the head from a falling stove pipe. He had had intermittent low back pain since playing college football in 1928-29.

The personal and family histories were not significant except for the death of his mother from Bright's disease, a history of Parkinson's disease in one brother at the age of 38 years, and the fact that another brother is ambidextrous. He is moderate in all habits, drinking wine but not smoking.

On admission, the patient was comatose and vomiting. The pupil of the right eye was larger than that of the left, but both reacted to light. Both fundi were reported negative. There was a conjugate deviation of the eyes to the right and up. There was a right hemiplegia with increased tendon reflexes, absent abdominal reflexes, and a central facial palsy on the right. Spinal fluid on admission revealed 40 mg. total protein, negative serology, and no R.B.C.

An eye examination two days later showed the pupils to be two mm. in diameter; they reacted to light. There was a conjugate deviation to the right; the eyes were without reflex motion when the head was turned. The right fundus showed a sharply outlined, pale disc with constricted arteries and dilated veins. The left fundus showed a pale choked disc with constricted arteries disappearing in a swollen retina. There were no hemorrhages. The left eye was proptosed.

On January 16th, 11 days after admission, the swelling in the left retina had partially subsided and hemorrhages were seen for the first time on and adjacent to the disc. On January 26th, the right pupil reacted to light; the left was fixed to light but reacted consensually. There was a slight left proptosis. The right fundus was negative. The left fundus showed marked edema of the entire central area with one large and several smaller hemorrhages overlying the disc and several round hemorrhages in the periphery. The caliber of the veins was variable while the arteries were markedly attenuated.

The patient regained consciousness on February 10, 1947. He had a marked right hemiplegia with a right facial paralysis, aphasia, apraxia, agnosia, and a blind left eye. His blood pressure at this time was 110/80 mm. Hg. He was no longer incontinent and could walk with help. He was discharged on March 18, 1947, with a diagnosis of cerebral thrombosis of the left middle cerebral artery and a right hemiplegia.

Nine months later, he was readmitted be-

cause of a convulsion. Spinal-fluid examination at this time revealed a clear colorless fluid under a pressure of 200 mm. Hg with a total protein of 95 mg. No R.B.C. were seen. Eye examination at this time revealed a slight narrowing of the arterioles of the retina in the left eye with one moderate-sized area of healed retinitis. His hemiplegia, and aphasia persisted.

On October 12, 1948, he was admitted to Birmingham Veterans Administration Hospital for speech rehabilitation. Vision was: O.D., -20/40, correctible to 20/20 with a -1.0D. sph.; O.S., blind, with no light projection or perception. The right pupil reacted to light directly but not consensually while the left reacted consensually but not directly. Visual fields revealed a right hemianopia in the right eye and a blind left eye (fig. 1).

The right disc was of normal color with no atrophy. Its center was elevated and the surrounding pigment epithelium was atrophic. Below the disc were two small round hemorrhages. The reflex from the arterioles was widened.

In the left eye, the entire posterior pole was occupied by a dense white mass of fibrous tissue, stellate in shape, and extending in all directions, covering the macula and nervehead in a diffuse sheet (fig. 2). Fibrous tissue extended along and sheathed all the vessels and extended into the vitreous. There was a broad band of fibrous tissue extending inferiorly from the nervehead in the center of which was a wide dark mass, apparently pigment or unabsorbed hemorrhage. Scattered round hemorrhages were also present.

His ophthalmic diagnosis was: Retinitis proliferans, secondary to intraocular hemorrhage; right hemianopia, secondary to a cerebral vascular accident. The neurologic department made the following diagnosis: Visual and auditory agnosia, agraphia, motor aphasia, dyscalculia, alexia, auditory loss, bilateral, dysmusia, and weak spatial orientation. While taking speech training, the patient developed a thrombophlebitis of the deep veins of his left leg. This responded satisfactorily to dicumarol and penicillin.

## Discussion

When this patient was first seen in the eye clinic at this hospital, it was the opinion of the staff that the eye findings were un-

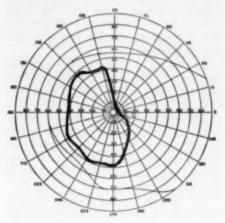


Fig. 1 (Goodman). Field study of the right eye shows a right hemianopia. (The left eye was completely blind with no light perception or projection.)

doubtedly the result of a massive subarachnoid hemorrhage. This view, however, became untenable when the records from the hospital where he had originally been treated were reviewed and it was learned that his spinal fluid had never shown any blood.

The sudden onset of this massive cerebrovascular accident in a relatively young man with no history of trauma, hypertension, or other vascular disease would certainly make one suspect a ruptured basal aneurysm. Since the circle of Willis lies in the subarachnoid space at the base of the brain, it is hardly conceivable that there could be such a massive hemorrhage in this area and the spinal fluid still be clear. The absence of cranial nerve palsies is also against the diagnosis of massive subarachnoid hemorrhage, since the third, fourth, and sixth nerves run through the subarachnoid space for part of their course.

The source of the hemorrhage, and it

probably was a hemorrhage instead of a thrombosis in view of the signs of cerebral compression, was in all probability a ruptured aneurysm of the left middle cerebral artery with involvement of the left internal capsule. A homonymous hemianopia is common in such lesions due to involvement of the sublenticular portion of the capsule and optic radiations. <sup>18</sup> How the posterior portion of the capsule escaped injury is not known but the patient never displayed any evidence of hemianesthesia. The blind left eye, a perfect example of an amaurotic pupil, if it were not blind would undoubtedly share in the hemianopia.

The occurrence of conjugate deviation to the contralateral side is difficult to explain. According to Cogan, a destructive lesion in the frontal area produces a conjugate deviation to the side of the lesion; whereas, an irritative lesion produces a deviation to the contralateral side. The frontopontine fibers concerned in conjugate eye movements pass through the anterior arm of the internal capsule in apposition to the supranuclear fibers for the facial muscles.

Walsh <sup>15</sup> states that a separate artery (Heubner's) reaches the anterior limb of the internal capsule and would thus supply the frontopontine fibers. It is entirely possible that the hemorrhage did not occur far enough anteriorly to produce destruction of the frontal eye area but was far enough to produce irritation and thus a deviation to the opposite side.

Since there was no blood in the spinal fluid, the intraocular hemorrhage cannot be explained on the basis of a subarachnoid hemorrhage. In keeping with Ballantyne's concept,<sup>2</sup> there probably was a sudden distention of the brain substance by the intracerebral rupture of a congenital aneurysm; this was sufficient to cause sudden compression of the veins and sinuses draining the eye and orbit and thus account for the intraocular and intraorbital hemorrhages.

724 South Victory Boulevard.

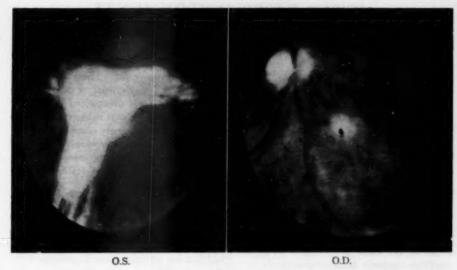


Fig. 2 (Goodman). The right fundus shows a disc of normal color with an elevated center. The surrounding pigment epithelium is atrophic. Below the disc are two small, round hemorrhages. The left fundus shows a dense white mass of fibrous tissue covering the nervehead and macula, sheathing the retinal vessels and extending into the vitreous.

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## NOTES, CASES, INSTRUMENTS

## EPIDEMIC KERATOCONJUNCTIVITIS\*

REPORT OF A SMALL OFFICE OUTBREAK

O. J. PELLITTERI, M.D., AND J. J. FRIED, M.D. New York

Epidemic keratoconjunctivitis was first reported by L. C. Hobson¹ in 1936. He described 16 cases in San Fernando, California, and called the condition punctate keratitis. In 1942, W. J. Holmes¹ reported an epidemic of about 10,000 cases which had occurred in Hawaii during the two preceding years. Hogan and Crawford³ studied an outbreak of 125 cases in 1942 and called the condition epidemic keratoconjunctivitis.

In the same year, Murray Sanders' announced the isolation of a virus from patients with the disease, by passage of conjunctival scrapings in mouse brain followed by growth in tissue culture. Neutralization with convalescent human serum was successful.<sup>5</sup>

In 1943, Perkins<sup>6</sup> and others reported an outbreak of the disease in a factory in upper New York state and suggested the possibility of the existence of carriers. The total number of cases was not given in the article, at the request of military authorities. Korns, Sanders, and Alexander<sup>7</sup> correlated the epidemiologic data and the neutralization tests in 101 cases in that epidemic. Positive neutralization tests were obtained beginning 6 to 10 weeks after onset of illness. The authors state that the test is not too sensitive and reactions are significant only in high dilutions. Braley reviewed the literature in 1943 and stated that convalescent serum, given early in the disease, seemed to prevent opacities.

## DESCRIPTION OF OUTBREAK

The outbreak herein reported consists of 24 cases. The first case occurred on September 15, 1948, and the last case on October 28, 1948. In this period 24 cases occurred. All were seen in the office of one of us, a practicing ophthalmologist. There were nine males and 15 females, most of them middleaged persons. Their occupations varied and appeared to play no part in the transmission of the infection. The only common factor in 19 of the cases was a previous visit to the ophthalmologist's office; the other four were household contacts to cases (table 1). Case 1 was the probable source.

### INCUBATION PERIOD

The first patient was seen in the ophthalmologist's office on September 21, 1948. He had had his infection since September 15th. Cases 2 to 20 came to the office for various eye conditions, not related to epidemic keratoconjunctivitis, on various days between September 21st and October 8th. The dates of their visits are given in Table 1. Following the initial visit, all developed symptoms of keratoconjunctivitis in from 3 to 19 days. One patient, 3, visited the office on September 20th, prior to the visit of the source case. However, she was operated on and examined daily by the ophthalmologist until September 28th, when she developed symptoms. The four secondary cases developed symptoms in 1, 18, 13, and 14 days, respectively, after initial exposure to a case in the household.

### CLINICAL SYMPTOMS

A profuse serous discharge from the eye was the first symptom. This never became purulent. The eyelids were swollen and patients complained of a feeling of a foreign body in the eye. Edema of the eyelids was so marked in some of the cases that the eyes could not be opened and the lids took on a glassy and blown-up appearance. Ecchymosis and occasional marked suffusion of the lids were not uncommon. In some patients only one eye was involved, in others, both eyes. Mild constitutional symptoms were present

<sup>&</sup>lt;sup>6</sup> From the Bureau of Preventable Diseases, New York City Department of Health.

TABLE 1\*
Cases of epidemic keratoconjunctivitis

Case No.	Name	Sex	Age	Occupation	Onset	Date of Previous Visit to Office	Number of Days from Visit to Onset	Known Exposure Outside Doctor's Office
1	H.D.	M	60	Tailor	9/15/48			None—visited office 9/21
2	G.K.	M	77	Artist	9/25/48	9/21/48	5	None
3	A.G.	F	60	Hotel Maid	9/28/48	9/20/48	8	Was operated upon in Hosp 9/21/48, seen by the M.D daily
4	S.S.	M	30	Carpenter	10/ 1/48	9/27/48	5	None
5	F.L.	F	50	Factory	10/ 2/48	9/28/48	5	None
5 6 7 8	A.P.	F	48	Housewife	10/ 2/48	9/30/48	3	None
7	D.R.	F	30	Hostess	10/ 2/48	9/21/48	12	None
8	J.P.	M	68	Retired	10/ 2/48	9/21/48	12	None
9	S.R.	F	60	Cafeteria help	10/ 2/48	9/21/48	12	None
10	H.S.	M	32	Salesman	10/4/48	9/28/48	7	None
11	A.G.	F	65	Housewife	16/ 6/48	9/28/48	9	None
12	F.W.	F	74	Housewife	10/6/48	9/21/48	16	None
13	F.W.	F	22	Secretary	10/6/48	10/ 2/48	5	None
14	C.W.	F	47	Housewife	10/8/48	10/ 2/48	7	None
15	H.M.	M	54	Clerk	10/ 9/48	9/21/48	19	None
16	L.C.	F	54	Housewife	10/10/48	10/ 2/48	9	None
17	E.R.	M	65	Clerk	10/14/48	10/ 2/48	13	None
18	H.B.	F	59	Housewife	10/14/48	10/ 4/48	11	None
19	J.P.	M	56	Baker	10/16/48	9/28/48	19	None
20	L.Z.	M	55	Storekerper	10/19/48	10/8/49	12	None
21	Mrs. M	F	54	Housewife	10/10/48	1		Contact to No. 15
22	Mrs. K	F	47	Housewife	10/13/48			Contact to No. 2
23	Mrs. R	F	50	Housewife	10/27/28			Contact to No. 17
24	S.D.	F	26	Housewife	10/28/48			Contact to No. 17

Cases 2 to 20 probably had their source in the physician's office.
 Cases 22 to 24 probably had their source as a result of contact in the home

such as low-grade fever, headache, malaise. Swelling of the preauricular nodes was noted in the first 24 to 72 hours, occasionally they were tender to pressure. In three cases, submaxillary adenopathy was also noted.

About 24 to 48 hours following the onset, the palpebral conjunctiva became red and swollen and the follicles appeared enlarged. Considerable chemosis of the bulbar conjunctiva was noted. A thin, delicate darkgray membrane occasionally lined the palpebral conjunctiva, After about a week, a gradual regression of the swelling began, the discharge diminished, the eyes felt less heavy, the conjunctival surface became smooth, and the patients said they felt better.

Corneal infiltrations were seen early in the disease. They were more in the periphery of the pupil and less in the pupillary center. The subepithelial infiltrations were sometimes shallow, giving the appearance of an ulcer, although, actually, no ulceration occurred. Gradually there was a regression, which continued for months. The corneal opacities caused considerable visual impairment for 5 to 8 weeks but the final visual acuity was good.

## LABORATORY FINDINGS

Conjunctival scrapings were made in 10 cases. Smears showed absence of inclusion bodies and microörganisms. There were many plasma cells, very few leukocytes, and a small number of epithelial cells. Neutralization tests of the sera from nine patients were done through the courtesy of Dr. Alson Braley, of Presbyterian Hospital. In five, the blood was obtained from 14 to 20 days after onset of illness; all sera gave a negative test. In four cases blood was obtained from 21 to 31 days after onset. All of these were positive by the neutralization test (table 2).

Blood was obtained from the physician and his office nurse, both of whom were asymptomatic. The specimens were tested by the neutralization method and found to be negative.

## TREATMENT

In addition to symptomatic treatment, such as the use of compresses and antiseptic ointments of sulfonamides, topical solutions and intramuscular injections of penicillin and a salve containing the borate salt of aureomycin were used. Four patients were also treated with blood from convalescent patients. No benefit appeared to result from any of these treatments.

## CONTROL

Control measures were instituted October 8th. These consisted in the use of separate syringes and eye droppers for each patient, sterilized after use, and thorough handwashing by the physician and his nurse between examinations. The patients were cautioned not to touch anything but personal articles while in the office, and to use tissues instead of handkerchiefs, as well as individual towels, pillow covers, bed sheets, and eating utensils.

### DISCUSSION

The epidemiology of epidemic keratoconjunctivitis has not been worked out completely. The causative agent is believed to be a virus but its properties are not well known. The interrelationship between the host, virus, and environment has not been worked out. The reason why only 10 to 20 percent of contacts became clinical cases has not been determined. Apparently the various factors which come into play in the epidemiology of other diseases are also operative in epidemic keratoconjunctivitis. It is evident that once a focus of infection has established itself, a certain percentage of contacts will develop clinical symptoms.

Sporadic cases of epidemic keratoconjunctivitis or small outbreaks in the New York area are rarely reported. In 1943, the disease was first made reportable in New York City. This was soon after the clinical syndrome was given tremendous amounts of newspaper and radio publicity. During that year there were reported 117 cases of the city. From 1944 to 1948, only 49 cases were reported.

It is felt that the incidence of epidemic keratoconjunctivitis is much higher than the reported number of cases would lead one to believe. Many cases are probably not reported, a certain number are misdiagnosed. In reviewing investigations of eye infections reported to the health department in the past, a large outbreak was found to have occurred previous to the newspaper notoriety given to the illness.

Between 1941 and 1943, in the Williamsburg-Greenpoint and Bedford areas of the

TABLE 2
RESULTS OF NEUTRALIZATION TESTS OF CASES OF EPIDEMIC KERATOCONJUNCTIVITIS

Case No.	Date of Onset	Date Blood Removed	No. Days after Onset	Results of Test
4	10/ 2/48	10/15/48	14	Negative
3	9/28/48	10/15/48	18	Negative
7	10/ 2/48	10/15/48	14	Negative
8	10/ 2/48	10/15/48	14	Negative
21	10/10/48	11/ 9/48	31	1500 neut, units
20	10/19/48	11/ 9/48	31 22	10,000 neut. units
Dr. J.J.F.		11/ 9/48	Asymptomatic	Negative
D.E.		11/ 9/48	Asymptomatic	Suspicious
(Office nurse)		, -,		
22	10/13/48	11/ 2/48	21	1500 units
15	10/ 9/48	11/ 9/48	31	1500 units
17	10/14/48	11/ 2/48	31 20	Negative

Borough of Brooklyn, there were approximately 600 to 800 cases of an inflammatory eye condition in the children of four public schools and one parochial school. Various diagnoses were made. At the beginning of 1943, with the clinical emphasis given to keratoconjunctivitis, the early cases were rechecked and in many, evidence of keratitis was found. It is probable that these were cases of epidemic keratoconjunctivitis. It would not be surprising if many small epidemics of the illness in institutions and offices of ophthalmologists go unrecognized. The possibility that a carrier state may exist has been discussed by Perkins.<sup>6</sup>

## SUMMARY

A small outbreak of epidemic keratoconjunctivitis totaling 24 cases has been described. The outbreak was localized in a physician's office specializing in ophthalmology. Clinical findings of a rapidly occurring conjunctival inflammation followed by keratitis which resulted in corneal opacities were confirmed in some of the cases by laboratory tests. The source of the epidemic was apparently a patient, and spread occurred in the office of the ophthalmologist. Simple control measures appeared to stop the further spread of the disease.

125 Worth Street.

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## EFFECT OF TILTED LENSES\*

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Every ophthalmologist knows that when a spherical lens is tilted so that it is oblique to the incident light it acts like a sphero-cylinder. It gains in spherical power and also acquires a cylindric element. A cylindric lens when similarly tilted becomes a stronger cylinder. The change in power naturally depends upon the strength of the sphere or cylinder used and upon the size of the angle of rotation. There are several more or less complicated formulas for finding the change

in power, but there is a simple method for getting the results with a minimum of formulas.

Suppose a +4.0D, sph. is rotated on a vertical axis through any angle, "a." Let D stand for the power of the lens,  $D_1$  and  $D_2$  for the resultant powers in the two principal meridians, these being the vertical and horizontal in our example. Let  $D_1$  stand for the new power in the vertical meridian, that is in the meridian of the axis of rotation, and  $D_2$  for the power at right angles.  $D_1 - D$  equals the increase of spherical power,  $D_2 - D_1$ ; that is, the difference between the two resultant powers, will give the power of the new cylinder. The axis of the cylinder developed will correspond to the axis on which

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the lens has been rotated, "a" stands for the angle of rotation.

The increase of spherical power is very easily found, as it is a percentage of the original power. The increase is equal to the square of the first digit of the value of the angle "a" taken in 10-degree intervals, that is the square of the number after dropping the zero. Thus if "a" is 10 degrees, the increase is 1-square percent = 1 percent. If "a" is 20 degrees, the increase is 2-square percent = 4 percent. If "a" is 30 degrees, the increase is 3-square percent = 9 percent. If "a" is 40 degrees, the increase is 4-square percent = 16 percent. If "a" is 50 degrees, the increase is 5-square percent = 25 percent.

Thus  $D_1 = D$  + the percent of D corresponding to the angle. For example, for D = 4.0, if "a" is 10 degrees,  $D_1 = 4 + 1$  percent of 4 = 4.04, for "a" = 20 degrees,  $D_1 = 4 + 4$  percent of 4 = 4.16. The same holds true for any power of D whether plus or minus.

After D<sub>1</sub> is thus obtained by a simple mental calculation, D2 is obtained from the formula  $D_2 = D_1/\cos^2 a$ . The stronger power is found by dividing D<sub>1</sub> by the cosine square of angle "a". Thus for D = 4.00 and "a" = 30 degrees;  $D_1 = 4. + 9$  percent of 4. =4.36.  $D_2 = 4.36/\cos^2 30 = 4.36/0.75 = 5.81$ . The cylindric value is  $D_3 - D_1 = 5.81 -$ 4.36 = 1.45. Thus a 4.0D, sph. turned on a vertical axis through an angle of 30 degrees becomes a +4.36D, sph. +1.45D, cyl. ax,  $90^{\circ}$ . One more illustration, say a +3.0D. lens is tilted on a horizontal axis through an angle of 40 degrees:  $D_1 = 3 + 16$  percent of 3 = 3.48,  $D_2 = 3.48/\cos^2 40 = 3.48/$ 0.5868 = 5.93. The cylindric element equals 5.93 - 3.48 = 2.45. Therefore lens now equals +3.48D. sph. +2.45D. cyl. ax. 180°.

When a cylinder lens is tilted on its power meridian, that is, the axis of rotation is at right angles to the cylinder axis, the resultant increase of cylinder power is very slight and negligible. But when tilted on its own axis as the axis of rotation, the increase in power is considerable. Thus a +3.0D. cyl. ax. 90°, tilted on a horizontal axis acquires very little increase of power. But when tilted on a vertical axis it becomes a considerably stronger cylinder. The increase in cylindric power can be found by the same method used for spheres, except that D<sub>2</sub> here is the full power of the resultant cylinder.

For example, suppose a 3.0D. cyl. ax. 90° is turned through an angle of 20 degrees on a vertical axis. First we find  $D_1$  as if the lens were a sphere, by adding the proper percentage. For "a" = 20 degrees, add 4 percent therefore:  $D_1 = 3 + 4$  percent of 3. = 3.12.  $D_2$  is then found as before:  $D_2 = D_1/\cos^2 a = 3.12/\cos^2 20 = 3.12/0.883 = 3.53$ . That is a 3.0D. cyl. ax. 90° rotated through an angle of 20 degrees on a vertical axis becomes a 3.53D, cyl. ax. 90°.

For angles between the 10-degree intervals, such as 15 degrees, 25 degrees, and so forth, we take the average of the two percentages for the angles above and below. Thus for "a" = 15 degrees, we take the average of "a" = 10 degrees and "a" = 20

degrees. This gives  $\frac{1+4}{2} = 2.5$ , we drop

the 0.5 and use 2 percent as the percentage increase in finding D<sub>1</sub>. For 25 degrees, we take the average between 20 degrees and 30

degrees, thus  $\frac{4+9}{2} = 6.5$ , drop the 0.5 and

we get 6 percent. For 35 degrees, we use the average between 30 and 40, and get  $\frac{9+16}{2}$  =

12.5, therefore 12 percent. For 45 degrees, we use the average between 40 and 50, and

get  $\frac{16+25}{2} = 20.5$ , therefore 20 percent.

Thus if a -5.0D, cyl, ax.  $180^{\circ}$  is tilted on a horizontal axis through an angle of 25 degrees, the change in cylinder power is found as follows. The percentage addition for "a" = 25 degrees lies between 20 degrees

and 30 degrees, and is  $\frac{4+9}{2}$  = 6.5, therefore 6 percent. D<sub>1</sub> = -5. + 6% of (-5) = -5.30, D<sub>2</sub> = -5.30/cos<sup>2</sup>25 = -5.30/0.8214 = -6.45D, cyl, ax. 180°.

## SUMMARY

A simple method is presented for finding the changes taking place when a sphere or cylinder is tilted or rotated on an axis so as to be oblique to the incident light. The increase in the spherical power resulting from the tilt is found by using a percentage number derived from the angle of rotation. The cylindric element developed is then derived from this value by a simple formula. The increase in the cylinder power resulting from a tilted cylinder is found in the same way.

37 West 97th Street (25).

## FISTULIZING "HALF-ELLIOT" OPERATION FOR GLAUCOMA\*

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All fistulizing operations for the treatment of simple glaucoma are based on the creation of a fistula under the conjunctiva which provides for a continuous outflow of the intraocular fluid. This is usually accomplished by resection of a small part of the sclera, thus providing an opening.

The only available and convenient area for this operation is a narrow border of the sclera above the limbus, limited in extent by the insertion of the ciliary body which is a ring, 0.85 mm. in width. The ciliary body should be left intact, and the cornea must also be protected. Incision of the edge of the sclera by the Lagrange method necessitates a wide incision, 8 to 10 mm., which may be dangerous in case of intraocular hypertension. Retroretinal expulsive hemorrhage may be precipitated which may result in enucleation.

In order to avoid this large incision, Elliot recommended a resection in the form of a disc made by a trephine, 1.5 mm, in diameter. In order to avoid scratching the ciliary body, Elliot excised a part of the corneal limbus, and instances of this disc falling into the anterior chamber have been reported.

While the corneoscleral opening is healing, it is covered by a thin film of corneal conjunctiva, in fact by an overgrowth of epithelium, which may easily cause inflammation in the presence of an ordinary conjunctivitis (infectio tardiva).

In the operation which I propose, the best features of the Lagrange and Elliot operations are combined. Excision is exclusively in the sclera (sclerectomy) using Elliot's small opening. This procedure avoids the misfortunes of both methods.

I use a larger trephine, 3.0 mm. in diameter, and, in order to prevent slipping, the trephine is supported by a needle. The trephine cut in not perpendicular but inclined. A half-disc is cut by drilling with one side of the trephine, hence the name of the operation. The resulting excised half-disc from the sclera is equal in size to the Lagrange excision (3.0 by 0.75 mm.).

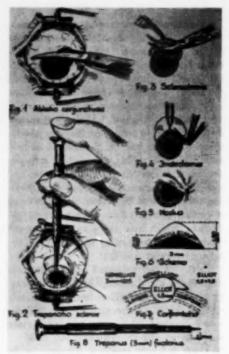
## TECHNIQUE

The conjunctival pouch is anesthetized by injection of novocain combined with epinephrine. The swollen conjunctiva is held with forceps (fig. 1) and an incision is made with curved and blunt scissors at the edge of the limbus. The conjunctiva is separated upward and sideward.

A suture (fig. 2) should be placed immediately but not tied. The exact positioning of the trephine in the area of the limbus parallel to the iris and its proper insertion

<sup>\*</sup> Elliot's operation is a corneoscleral resection of a disc, 1.5 mm. in diameter. The "half-Elliot" operation herein described is a scleral resection of a half-disc, 0.75 by 3.0 mm. in diameter.

<sup>†</sup> Formerly professor of ophthalmology, University of Vilna.



Figs. 1 to 8 (Szymański). Technique of the "half-Elliot" operation.

are essential to avoid damage to the ciliary body while drilling. If the instrument inclines too far forward, the lens capsule may be destroyed; if it inclines too far backward, the incision will be too narrow. The trephine needle should, therefore, be inserted in the uncovered limbus, protruding in the very center of the arc so that it is visible behind the cornea and in front of the iris.

As the chamber is opened, liquid flows out and there is a spontaneous rise of the iris. At this moment, the patient feels a slight pain. Drilling should be continued until the limbus is reached, at which moment the instrument is withdrawn, being held parallel to the iris.

After the trephine is removed (fig. 3), the scleral segment, the shape of a uvula, inclines backward, showing the dark opening. After the sclerotomy has been performed, the uvula is caught by iris forceps and is cut at its limbal base by means of Lagrange scissors or Graefe knife (sclerectomy).

As the iris becomes visible in the opening (fig. 4), it should be handled with straight iris forceps, raised, and cut off with iris scissors.

Finally (fig. 5), the suture is tied at the temporal side, and a conjunctival flap is used to cover the wound.

For over 20 years, I have used this "half-Elliot" operation in cases of simple glaucoma, as well as in buphthalmos and in opticnerve atrophy.\* In over 500 cases treated at the Vilna University Clinic, no more than one percent of complications, such as iridocyclitis, have been encountered.

University of Paraná.

### OPHTHALMIC MINIATURE

Those who are unacquainted with the anatomy of the eye can only acquire this knowledge perfectly by dissections, which should be repeated on the dead eyes of animals; but particularly of the human subject. A few dissections will impress the mind with more complete ideas of the eye than a thousand written descriptions.

A Treatise on 118 Principle Diseases of the Eyes and Eyelids, William Rowley, London, 1790.

<sup>•</sup> Since, in optic-nerve atrophy, the blood pressure is usually lower and the normal intraocular pressure is relatively higher, a fistulizing operation will improve the alimentation of the fundus oculi.

## SOCIETY PROCEEDINGS

Edited by DONALD J. LYLE, M.D.

## CHICAGO OPHTHALMOLOGICAL SOCIETY

November 21, 1949

DR. DERRICK VAIL, president

CLINICAL MEETING

Presented by the Departments of Ophthalmology, Hines Hospital, and Strich School of Medicine, Loyola University

Persistence of hyaloid and retrolental fibroplasia

DR. DAVID B. MAHER presented B. S., born prematurely on December 22, 1947, with a birth weight of 2 lbs., 13 oz. She was hospitalized for two months and was first seen by the ophthalmologic service on June 11, 1948, at which time microphthalmos and photophobia were noted and a membrane on the posterior surface of the lens was seen, more extensive in the right eye. A diagnosis of retrolental fibroplasia was made. The eyes were put on a miotic (pilocarpine, one percent, twice daily). Once a week the pupils were dilated, to prevent synechias, with a combined mydriatic consisting of homatropine (one percent), euphthalmine (two percent), cocaine (0.5 percent), and paredrine (one percent), as suggested by Terry.

Examination under ether anesthetic showed a weblike membrane on the posterior surface of both lenses. Cloquet's canal was occupied by a fibrous vascular cone extending to the disc. The margins of the disc were clear. There was no evidence of retinal detachment or elongation of the ciliary processes.

Subsequent progress:

September 28, 1948—Doubtful following of light.

October 1, 1948—Grasping for objects. November 18, 1948—Definite following of light

March 8, 1949—Follows objects and holds them close to the left eye.

August 9, 1949—Definite evidence of visual attention.

November 9, 1949—Walks alone, grasps objects without hesitation. Esotropia constant. Fixes O.S. There has been no evident change in the physical findings O.U. since first examination.

Dr. David B. Maher said that the second case, J. M., born August 31, 1948, is presented in contrast to the previous child. J. M.'s birth weight was 2 lbs., 11 oz. She was first seen at the age of six months, at which time microphthalmos with complete membranes behind both lenses and elongation of ciliary processes were noted.

Unfortunately neither case was seen during the stage of development of the retrolental fibroplasia. In none of the cases reported by Owens (Am. J. Ophth., 32:1 (Jan.) 1949) was there persistence of the hyaloid system.

In a more recent series reported by Gilger (Am. J. Ophth., 32:917 (July) 1949), in which development of the fibroplasia was observed, none had a hyaloid artery or a posterior tunica vasculosa lentis or remnants present after the first two weeks of life.

These two cases are presented because it is felt that the first represents persistence of the hyaloid vascular system and posterior tunica vasculosa, with probably proliferation of the glial tissue of Bergmeister's papilla; whereas, the second case may well be one which developed according to the process observed by Owens and Gilger.

Discussion. Dr. Milton M. Scheffler mentioned that the first case is similar to that described by Reese as persistence of the primary vitreous. In a recent paper he suggested that there were two types of cases grouped under tunica vasculosa lentis. The first group he considered as persistence of the primary vitreous, in which the vascular membrane lies on the posterior lens surface and is directed backward along Cloquet's canal toward the papilla. The retina and macula in these cases are intact, and vision may be expected to improve as the membrane absorbs. This type of case was shown pathologically. The gradual visual improvement of the first child may be explained as the result of continued absorption of the membrane behind the lens.

The second group is similar to that reported by Owens and others. (Klien believes that because of a vascular component, the hemorrhages which develop become organized, resulting in retinal detachment. Vision naturally fails in these cases.)

## PSEUDO-ALBUMINURIC RETINOPATHY

Dr. R. L. Cannon presented C. A. S., who had a case of pseudo-albuminuric retinopathy, as described by Leber. The patient stated that his eyes had been all right until five days prior to admission to Hines Hospital, when he noted fogging of vision in the left eye.

Physical examination was essentially negative except for vision in the left eye, 4/400, not improved by pinhole or refraction. Extraocular muscles were normal, and external examination was negative. The fundus of the right eye was normal, but that of the left eye showed marked blurring of the disc margins and about two diopters of elevation of the disc. There were no retinal hemorrhages. The retinal arteries showed some increase in reflex stripes and some A.V. compression. There was retinal edema in the macular area with spokelike linear exudates radiating from the macula.

Extensive laboratory examinations failed to reveal any significant findings, except for increase in the agglutination titer of paratyphoid A, paratyphoid B, typhoid O, and typhoid H. The urine was negative. N.P.M., cholesterol, urea, uric acid, and creatinin of the blood were normal, thus ruling out nephritis.

The patient was transferred to the medical service to determine the status of the increased agglutination titer. While there, a subsequent history revealed that a few days prior to admission the patient had received an injection of triple typhoid vaccine intravenously. This was considered adequate explanation for the increase in agglutination titer.

Stereocampimeter examination revealed a central scotoma of the left eye with some peripheral contracture of the superior and nasal portions of the visual field. Under routine treatment for papillitis, there has been gradual absorption of the inflammatory process in the region of the disc, and of the star-shaped figure in the region of the macula, so that at this time the patient shows a temporal pallor, but still has the macular starlike figure. Vision at present is 20/400 with correction.

Final diagnosis: Papillitis, left eye, cause undetermined, and pseudo-albuminuric retinopathy, due to papillitis.

## SURGICAL PROCEDURE FOR GLAUCOMA

Dr. T. B. Schertz presented two cases to demonstrate a surgical procedure suggested by Sir Richard Cruise in an article in the *British Journal of Ophthalmology*, February, 1947. The intended purpose of the procedure is to provide an endothelial lined filtration tract which, as a result of the endothelial lining, becomes permanent.

The technique consists of preparing a limbus-based conjunctival flap, and slitting the cornea for a distance of about 2.0 mm. A 5.0-mm, scratch incision is made through the sclera, parallel with the limbus, and 1.0 mm, from the limbus. This provides an opening into the anterior chamber, close to the root of the iris. A 2.0-mm, incision is then made at each end of the original 5.0-mm, incision at about a 45-degree angle from the original incision, converging into the cornea so that a triangle is formed with a blunt apex in the cornea, which acts as a hinge. A flap thus prepared is free to move up and down. The conjunctival flap is then

replaced, and may or may not be approximated by three interrupted sutures.

An important phase of the procedure is to institute vigorous massage within 24 hours after surgery, and to continue this at intervals throughout every 24-hour period for several weeks, until endothelium from the posterior surface of the cornea has had time to line the filtration channel completely. Massaging forces the apex against the flap, forcing it to open and close, thus breaking up the fibroblasts which lie across the wound, before they have a chance to form permanent cicatrix.

The advantages of the procedure over sclerotomy or trephination are: (1) Formation of the endothelized tract, as previously described; (2) with the institution of massage, the flap provides a large surface and, therefore, more force for the aqueous to work against the strength of plasma and fibroblasts, which tend to seal an open wound; (3) the chance of secondary infection is diminished.

Case report. This 35-year-old man had had an iridectomy for acute congestive glaucoma, left eye. He had symptoms in the right eye only of halos when looking at a lighted match. There was no complaint of pain. Tension was: R.E., 63 mm. Hg (Schiøtz); L.E., 55 mm. Hg. (Schiøtz). Examination revealed that the patient had diabetes mellitus with rubeosis iridis and bilateral glaucoma.

Despite the grave prognosis of glaucoma and rubeosis iridis, with a complete capillary bed covering the entire filtration meshwork, surgery was attempted, inasmuch as no medical measures were successful in lowering the tension for more than a short time.

On September 23, 1949, a Wheeler combined cyclodialysis with iridectomy was performed with minimal hemorrhage. The tension, however, returned to 55 mm. Hg. On October 8, 1949, surface cyclodiathermy of the entire lower half of the globe was performed with subsequent reduction of tension which, however, again returned to 55 mm. Hg.

On November 8, 1949, the flap sclerotomy, suggested by Cruise was done and followed by massage in six hours. The present tension, two weeks postoperatively, is 34 mm. Hg (Schiøtz), showing a reduction of 2 to 6 mm. Hg following massage. Consistent recurring hyphemias are a problem in this case. The result of the diabetic changes forecasts an unfavorable prognosis.

Case 2 was that of a 51-year-old white man, also a diabetic, who had a tension of 46 mm. Hg (Schiøtz) in the left eye; a mature cataract was also present. There was no rubeosis iridis. Flap sclerotomy was performed on November 17, 1949, and massage was instituted within six hours. In this case, hemorrhage occurred into the anterior chamber, but was minimal and remained a problem for only about 48 hours. The eye showed much less reaction, and signs of organized hyphemia in the filtration area were not evident. The present tension is 28 mm. Hg (Schiøtz), and massage produces an average lowering of tension of 6.0 mm. Hg.

Both these cases have obviously been operated on too recently to demonstrate anything conclusively, and were presented merely for demonstration of the technique.

Discussion, Dr. Max M. Kulvin said that the first case operated on by this technique was done a year ago, and did not work; later it was found that massage of the eye had not been done, which is an important point. In the cases presented, massage was started within the first few hours and tension remained down except at night. Therefore, massage has been done at night, and there is no morning rise of tension. The procedure is offered as a possibility when other operations have been unsuccessful. Cruise and Boxhill have performed the operation with good results. Possibly their classification of cases is different, and these may not be suitable cases.

Dr. Daniel Snydacker said that the greatest single difficulty with all types of filtration operations is that the filtering scar has a tendency to heal firmly and close completely. In Cruise's original article there was no claim that the flap kept flapping but, as here indicated, an epithelial lining formed in the scar to keep a fistula open. Massage alone can hardly keep an incision open, and it is probable that the majority of these flap sclerotomies will heal firmly and not be effective.

## CHORIONEPITHELIOMA OF CHOROID

Dr. Max M, Kulvin presented a case of chorionepithelioma of the choroid, metastatic from a tumor of the testicle. The patient, a white man, aged 22 years, was admitted to Hines Hospital on February 29, 1948, with the history of removal of the left testicle and X-ray therapy to the left groin in March and April, 1947. The tumor was found to be an adenocarcinoma.

He was relatively symptom free until about six weeks before admission to Hines Hospital when he first noticed onset of pain in the region of the left upper quadrant. The first eye examination showed visual acuity of: R.E., 20/15; L.E., 5/400, uncorrectible, Tension was: R.E., 10 mm. Hg (Schiøtz); L.E., 13 mm. Hg. The right fundus was normal, Examination of the left fundus showed a two-diopter elevation of the retina two disc diameters temporal to the nervehead.

A diagnosis of tumor of the choroid, metastatic, with detachment of the retina was made. Enucleation of the eye was advised. However, the patient's general condition became increasingly more serious and he died on September 5, 1948.

Autopsy studies revealed metastasis throughout the body. The pathologic report of the Army Institute of Pathology on the left eye was:

Gross. The specimen revealed a white oval mass, 16 by 19 by 12 mm. filling two thirds of the intraocular volume. The mass had detached the retina and was streaked with reddish areas. The subretinal space was partially filled with blood.

Histology. Extending from the posterior choroid into the subretinal space was a tumor composed of cells with vesicular, often nucleated, nuclei and a prominent chromatin network. A diagnosis of chorionepithelioma, metastatic in the eye from the testicle was made.

Discussion, Dr. Frederick A. Lloyd: This paper probably has more interest for the pathologist, the general surgeon, and the urologist, than for the ophthalmologist, In treatment of malignant tumors today, there is a tendency to push morphology into the background and rely more upon biochemical, biologic studies. However, until the final therapy for carcinoma has been found, early radical surgery will be the treatment of choice. To place our indications properly and to arrive at a proper prognosis, there must be better understanding of the pathways and the mechanism of metastasis. A paper such as this adds to the sum total of our knowledge and helps in arriving at more proper conclusions.

Chorionepithelioma of the testes is an interesting tumor. The common location is in the uterus, and the prerequisite for development is the presence of a fertilized ovum. After fertilization has occurred and as the embryo is developing, there is in the ectoderm of the embryo a certain tissue known as trophoblastic tissue, which gives rise to the elements of the chorion. If chorionepithelioma develops, it elaborates the chorionic gonadotropic hormone which is secreted in the urine. It is mostly the luteinizing factor of this hormone, or prolan A, that is found in the urine. In many mixed tumors of the testes this same hormone is found, usually from zero to 3,000 units in the urine. In choriocarcinoma, however, this hormone appears in the urine in tremendous quantities, often as high as 75,000 to 150,000 units. This fact is frequently used in the proper diagnosis of so-called chorionepithelioma.

The question arises, why should a tumor of this sort appear in the male gonad or the testes? The tumor probably arises from the spermatogonia. These are pluri-potential

cells and have all the potenial qualities of forming tissue of any sort. For that reason they give to tumors; frequently these are mixed tumors, teratomas, and these chorionepitheliomatous elements may be found by careful examination, in certain of these mixed tumors.

In a series of 458 testicular tumors seen at Hines Hospital from 1931 to 1947, there were two chorionepitheliomas reported, both in 1947. This number is probably far too small, and that may be ascribed to the fact that the tissues were not examined thoroughly and carefully enough.

Testicular tumors are very malignant, and have a tendency to metastasize, mainly to the retroperitoneal lymph nodes. Metastases to the liver and the lungs may also occur. In the case of the chorionepithelioma we usually have a tumor in which there are extensive necroses and hemorrhage, due to the important fact that the cells of the chorionepithelioma have an affinity for the blood vessels. They invade the blood vessels; they soon produce obstruction, ischemic necrosis, and rupture of the vessel wall and hemorrhage. As a result the tumor is frequently reddish-brown in color and friable.

In the case shown, the chorionepitheliomatous elements appear in a teratoid or mixed tumor. There are metastases in the liver, with numerous reddish, hemorrhagic areas. The chorionepithelioma has a tendency, more than other testicular tumors, to metastasize by way of the blood stream.

Another interesting question arises with regard to the case presented by Dr. Kulvin—that is, what is the pathway of the metastasis from the testicle to the eye? Actually, tumors which appear in the peripheral tissues, which have to be reached by the peripheral circulation may, from an area such as the testes, reach the eye only by traversing the circulation of the lungs. Testicular tumors may metastasize to the retroperitoneal nodes. Then by way of the thoracic duct they reach the venous circulation, the right heart and, finally, the lungs. In that way they reach

the peripheral circulation—for example, through the ophthalmic artery, they reach the eye. Or, if they circulate through the spermatic circulation, the inferior vena cava, and again by the same pathway to the lung.

These tumors frequently present a great problem. Last year a roentgenologist at the Zurich Red Cross Hospital presented an interesting and classical monograph in which he explained a great many of the problematic peripheral metastases that occur. The book is known as Cancer Metastases and is the result of a 15-year study of cancer material at this hospital. The author, Hans Walther, came to some interesting and important conclusions which help us to understand better the mechanism of metastases from cancer.

He shows that, in some cases in which we had assumed certain bizarre and mystical pathways for spread of metastases, he could explain them actually upon the basis of normal lymphatic and blood vascular pathways. In some of these peripheral metastases—as, for example, to the eye—what actually happens is that metastases do occur to the lungs. They are so-called micrometastases. They are overlooked in ordinary autopsies and routine sections of the lung. But, if numerous step sections are made, these micrometastases are found.

From these, further metastases occur into the peripheral circulation and, in this way, metastases may occur from metastases by 2, 3, 4, sometimes even 5 stages. It is an interesting fact that from the lymph nodes, for example, the metastases do not have to go through the lymphatic circulation. The lymph node itself has an active and rich blood circulation, so that from the lymph node the metastases may leave via the venous drainage from the node and get into the main venous circulation, and in that way they eventually get into the main arterial circulation.

INTRAVENOUS TETRAETHYL AM MONIUM CHLORIDE

Dr. Arnold P. Drucker, Dr. Max S. Sadove, and Dr. Klaus R. Unna reported

on their study of the ocular manifestations of intravenous tetraethyl ammonium chloride (T.E.A.) in man.

T.E.A. acts as an autonomic ganglionic blocking agent, Besides lowering blood pressure and increasing the pulse rate, it affects ocular structures as an iridoplegic, a partially dilating mydriatic, and an efficient cycloplegic. It produces a rapid and profound reduction in intraocular pressure, but this is of short duration.

Discussion. Dr. Peter C. Kronfeld said that this paper gave a neat ophthalmic demonstration of the important pharmacologic principle that autonomic ganglia, parasympathetic as well as sympathetic, are blocked by the intravenous administration of quaternary ammonium compounds, Two of the findings are particularly interesting. One is the fact that the near and light reactions of the pupil were found to be equally inhibited. This finding conflicts with the prevailing views, according to which the peripheral efferent pathways for near reaction do not pass through the ciliary ganglion. This work indicates strongly that the pathway for the near reaction also goes through the ciliary ganglion. It is hoped that these studies will be continued. Interesting, too, is the drop in ocular tension observed by Dr. Drucker, and the careful way in which he interprets this phenomenon. He stated: "Blood pressure changes were not sufficient to account for the magnitude and rapidity of change of ocular tension." With this statement there can be no disagreement,

Since the effects of tetraethyl ammonium chloride are due to actions at multiple sites it is difficult, if not impossible, to say what the mechanism of the drop in tension is. Possibly it is hemodynamic. Coller and his associates at Ann Arbor have demonstrated a marked increase in blood flow and skin temperature during the first five minutes following injection of tetraethyl ammonium chloride. That is at the time when Dr. Drucker has observed the marked drop in ocular tension.

Those findings indicate that blood distribution is promptly and profoundly altered by injection of tetraethyl ammonium chloride. It deprives the entire vascular system of its vasomotor control. The impulses that travel down from the vasomotor centers are cut down completely and the vascular system has now to exist on the intrinsic or humoral factors. Under those conditions the distribution of blood is profoundly altered, which is the most probable cause of the drop in tension.

Dr. James E. Lebensohn: The activity of tetraethyl ammonium chloride on the ciliary ganglion adequately accounts for all ocular effects of the drug, including the lowering of ocular tension. The far-reaching hemodynamic mechanism that Dr. Kronfeld postulates is probably not a determining factor since pupillary dilatation, lowering of intraocular pressure, and deepening of the anterior chamber are just as effectively produced by procaine anesthesia of the ciliary ganglion. The dilated pupil from ganglion anesthesia also does not respond to the cholinesterase inhibitors such as eserine, prostigmine, or di-isopropyl fluorophosphate; but drugs that, like acetylcholine, act directly on the effector cells, such as pilocarpine, mecholyl, or furmethide, cause contraction.

It would certainly be preferable from the ophthalmologist's standpoint that the action of tetraethyl ammonium chloride be localized to the eye, and so avoid disturbing systemic manifestations. This could be accomplished by simple retrobulbar injection. When this is attempted, the incorporation of hyaluronidase would more surely assure infiltration of the ganglion. Localized injection of tetraethyl ammonium chloride about individual ganglia has already been done. Our fellow member, Dr. Blankstein of Milwaukee, has been injecting the superior cervical ganglion with this drug for the past two years.

Dr. Klaus R. Unna thought that Dr. Drucker's findings were of particular importance to a pharmacologist who is interested in all types of autonomic drugs and partic-

ularly in ganglionic blocking agents.

On systemic application of a ganglionic blocking agent in man, one is much surprised how difficult it is to predict the overall effects. By impeding transmission in both sympathetic and parasympathetic ganglia, the agent interferes with autonomic control of every organ system.

The use of tetraethyl ammonium is still in an experimental stage. It has been tested as a diagnostic agent in hypertension. In a normal person it has only a slightly lowering effect on the blood pressure combined with a slight increase in heart rate. These effects become more marked when the subject stands up. It looks as if the systemic effects on the cardiovascular system in normal and hypertensive men are more the expression of impairment or blockade in sympathetic ganglionic transmission than in parasympathetic.

Dr. Drucker's findings show that, in the eye, the effects on parasympathetic ganglia are much more evident than on the sympathetic. He tested some subjects also with a second ganglionic blocking agent, C5 or pentamethylene-bis (trimethyl ammonium iodide) with somewhat different results. It shows that one ganglionic blocking agent might produce results different from another. C5 is about 10 times as potent as T.E.A. in animals. Obviously, much more has to be learned about the systemic application of these new agents in man.

Not all ganglionic blocking agents have to be quaternary ammonium bases; there are others which have a somewhat different structure. We know only of agents which are of short duration and which cannot be given any other way but parenterally; they are too easily destroyed and we know from metabolic studies with tetraethyl ammonium that it is rapidly destroyed or excreted though the kidneys.

Dr. Arnold P. Drucker (in closing) said

that several interesting points have been brought out. Dr. Kronfeld mentioned the studies of the group at Ann Arbor—the filling effect upon the feet—and the subjects in this presentation complained similarly; it was one of their outstanding complaints, the tightness of the shoes and the sensation of filling of the vessels of the feet.

Dr. Lebensohn pointed out the effect of procaine to duplicate the tension-reducing effect of T.E.A. T.E.A. is not recommended for use on all patients; it is not a simple drug to handle. But in selected cases, when one has a good idea of the vasomotor status of the patient, it might be interesting and indeed very helpful.

The technique of examination is a neat trick. Refractions have been done on medical students and residents, individuals who are presumably mentally stable enough to accept some of the side effects previously described to them. They lie on a couch, and a mirror 10 feet away is used to reflect the chart overhead. The patient's head is turned to the side with the trial frame on, and thus it is possible to refract one eye above the other. It is a matter of orientation. It is no more difficult than in the upright position. Another possibility would be a chart on the ceiling with the patient lying below, looking up, and the examiner sitting above at his usual refracting and retinoscoping distance,

The use of T.E.A. is an excellent short procedure and the subjects have all been pleased with the results of refraction. The fact that they can be back at their work in less than an hour was especially gratifying. I assume that T.E.A. will have its greatest value as a cycloplegic in patients whose time is limited. It is in the young and physically stable individual that this drug should be used, and it is probably an ophthalmic curiosity as much as anything else.

Richard C. Gamble, Secretary.

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## THE 16TH INTERNATIONAL CONGRESS OF OPHTHALMOLOGY

The 16th International Congress of Ophthalmology was held in London, July 17th to 21st, under the presidency of Sir Stewart Duke-Elder. More than 1,200 full members and 800 associate members registered; 65 countries were represented.

It is not generally understood that the congress is sponsored by the International Council of Ophthalmology of which Professor Nordenson of Stockholm has been president. The International Council of Ophthalmology is composed of representatives of 16 national ophthalmologic societies and is concerned, apart from the international congress, with administrative and academic ophthalmic matters of international character. It held several meetings during the congress.

The congress, which is the oldest established medical event of its kind, is held nominally every four years. The last to be held was in Cairo, in 1937. Any attempt to describe in detail the excellent scientific program and the warmth of hospitality extended by our British colleagues would be doomed to failure.

The outstanding, detailed, perfectly ex-

ecuted arrangements were a tribute to the executive direction of Sir Stewart Duke-Elder and the organizing ability of Mr. Frank W. Law, the secretary-general. Quite obviously they had excellent cooperation from their committees. The carefully planned and entertaining events for the wives and children of the delegates were carried out under the direction of the charming and evergracious Lady Duke-Elder and her committee.

On the Sunday preceding the opening of the congress, a most impressive and inspiring memorial service was held for Sir William Bowman, at which Prof. J. W. Nordenson, the president of the international council, laid a wreath at the memorial tablet to Bowman in what remains of the bombed St. James's Church in Piccadilly.

The congress was opened formally on Monday morning by His Royal Highness, the Duke of Gloucester, Following the reading of greetings from Their Royal Highnesses, the King and Queen, the Duke of Gloucester reviewed what ophthalmology has done in the past and expressed hope that ever greater advances would be made in the future.

At the conclusion of the Duke of Gloucester's address, the first Gonin Medal was presented to Dr. H. Arruga of Barcelona by Professor Nordenson as president of the International Council.

Following Sir Stewart Duke-Elder's address of welcome, there were inaugural addresses of the representatives of the six continents: Dr. Edward Hartman, speaking for Europe; Dr. John H. Dunnington, for North America; Prof. R. Argañaraz, for South America; Sir Jenrshedji Duggan, for Asia; Dr. Abdel Fattah El Tobhy, for Africa; and Dr. J. Ringland Anderson, for Australia,

The scientific sessions were held in Friends House and in University College, Two of the outstanding features were the round-table discussions on "The role of the sympathetic system in the genesis of vascular hypertension and its effect upon the eye," and on "The clinical and social aspects of heredity in ophthalmology." In each of these roundtable discussions, 20 ophthalmologists participated. In addition, 131 individual papers were read, these being presented in three different halls. Space does not permit the listing of these excellent presentations.

Beside the scientific papers, there were more than 60 scientific films. The most spectacular of these was the one of Amsler of Switzerland, showing the reaction of cells from the aqueous to bacteria. In this film, the organisms were shown entering the cells and were followed in their work of destruction of the individual cells.

The official languages of the congress were English, French, and Spanish, with extensive arrangements having been made for translating and interpreting. In some instances, the speaker made announcements in all of the official languages.

Operative and other demonstrations were arranged, as well as exhibitions under the headings-clinico-pathologic, histologic, industrial, illuminating, scientific, and trade. The various exhibits were housed in the Wellcome Research Institution, the London School of Hygiene and Tropical Medicine, and St. Pancras Town Hall, all within easy walking distance of the registration office and bureau in the British Medical Association House.

During the congress, in addition to the meeting of the international council, there were meetings of the International Association for the Prevention of Blindness and the International Organization against Trachoma.

As is usually true, the social aspect of the congress was one of its features, and our British hosts arranged many unusual events. Preceding the congress, there were many tours in England and Scotland, and, during the congress, there were daily excursions about London.

On Sunday afternoon there was a reception at the Royal College of Surgeons and, on Monday night, the reception and dance of the congress took place, On Tuesday night there was a reception by His Majesty's Government at Tate Gallery. This was preceded by a cocktail party at the American Embassy for the visiting Americans. On Wednesday evening, a selected number of the delegates were entertained at dinner in the 400-yearold Apothecaries Hall in Blackfriars Lane by the officers of the Ophthalmological Society of the United Kingdom and the Faculty of Ophthalmology.

Following this, at a reception of the Royal College of Surgeons of England, Honorary Fellowships in the Royal College of Surgeons were conferred upon Jean-Pierre Bailliart of France and Derrick Vail of the United States.

On Thursday afternoon, a group of nine delegates was invited to a garden party at Buckingham Palace. The social activities ended with the official banquet of the congress on Thursday night.

From this brief account, it is quite apparent that the 16th International Congress of Ophthalmology will always be remembered as one of the most outstanding of all congresses and we, who had the privilege of attending, will always remember with a great deal of pleasure the warmth of hospitality and, above all, the graciousness of our British hosts.

Frederick C. Cordes.

## THE PINHOLE TEST

The pinhole is one of the most ancient, useful, and instructive of optical devices. The pinhole camera, invented by Porta nearly 400 years ago, is still the only means by which architects can obtain details of buildings entirely free from distortion. In ophthalmology the simple pinhole often rapidly indicates the basis of faulty vision.

This important screening test, though neglected by older authorities such as Roosa and Alger, is discussed in all recent texts on refraction but in insufficient detail. Duke-Elder, with characteristic accuracy and conciseness, states in his Textbook of Ophthalmology (volume IV): "In general, the stenopeic hole improves to a great extent visual defects due to refractive anomalies, to a less extent those due to abnormalities in the media, but does not ameliorate and may even aggravate those due to faulty perception."

In normal ocular refraction the pupillary area is filled with rays from each point of the object which, in turn, are refracted to a corresponding point on the retina. If the ocular refraction is not true, the retina truncates the image cone of rays and the sequential blur is in proportion to the diameter of the diffusion circles that now represent each point of the object. The prescribed lens lessens the diameter of the diffusion circles in accordance with the efficiency of the correction.

The pinhole, in contracting the base of the image cone, likewise reduces the diffusion circles. If the correction worn, although imperfect, improves the acuity, the pinhole over the glass gives better results than when placed before the naked eye since the glass has already aided in changing the slant of the image rays.

Good vision with the pinhole merely shows that the macula has normal function but does not imply that the perceptive apparatus is intact. I have observed a myope with 20/20 pinhole vision in an eye that had a detachment with hole in the superior temporal quadrant.

The reduction of light produced by the pinhole must be compensated by supplemental lighting of the chart to assure the fullest pinhole acuity. Bane demonstrated that the intensity of illumination normally determines the optimum-size pupil for best vision. With eyes under full mydriasis and cycloplegia but accurately corrected, the best acuity with high illumination was obtained with a 2.0-mm. artificial pupil but for low illumination the most efficient aperture was 8.0 mm. The minimal useful diameter of the stenopeic hole is set by diffraction. At 2.0 mm. this complicating factor is slight but,

when the diameter becomes less than 0.5 mm., a vitiating blur is evident. In Bane's clinical study the most effective pinhole varied in diameter between 0.94 and 1.75 mm., that at 1.32 mm. being most generally favored. The pinhole of the standard trial case has an aperture of 1.0 mm. The closer to the eye the opening is placed, the brighter the image and the less restricted the field of vision.

As the pinhole places the eye in almost universal depth of focus it may be used as a makeshift magnifier since the near point can be brought closer to the eye, making the retinal image correspondingly larger. When thus used, if the diameter of the pinhole be changed from 1.0 mm, to 0.2 mm., the effect of diffraction is easily demonstrated. The print is then too blurred to be distinguished; and if the aperture be further reduced, the entire page assumes a uniform grayish cast.

The precise correction of an uncomplicated refractive error should achieve an improvement of visual acuity that is as good if not better than the pinhole result. The pinhole gives no help in diffuse opacities of the media as occurs in edema of the cornea, epithelial dystrophy, extensive parenchymatous keratitis, mature cataract, and vitreous haze; but in irregular astigmatism, conical cornea, and discrete opacities of the cornea or lens, the improvement by the pinhole is sometimes very much better than is obtainable by the most meticulous correction. This results from the marked visual disturbance caused by light incident on slight obscurations of the refracting media.

The scattered light, spreading like a white crape over the macula, interferes with image discernment. Exclusion of peripheral light even with the hand is frequently beneficial. The pinhole, by cutting off the rays that reach the obscuration, limits the light pencil to that subject to regular refraction.

Finding better vision with the pinhole than can be elicited with lenses is hence a valuable diagnostic clue that locates the visual disturbance to the media. This is frequently noted in incipient cataract, especially with slight posterior opacities, where the lens change sometimes eludes detection by oblique illumination, loupe, or ophthalmoscope and can be observed only with the slitlamp.

In iridocyclitis, the pinhole improves the faulty vision when due to ciliary spasm, keratic precipitates, folds of Descemet's membrane, or pigmentary deposits on the lens but, if turbidity of the anterior vitreous is responsible, as often occurs, the pinhole causes no change or a decreased acuity.

A failure of the pinhole to improve vision indicates that the amblyopia cannot be benefited by glasses because of functional defect, imperfect perception, or structural change. When a macular lesion or impairment of the light sense is present, the pinhole diminishes visual acuity by its reduction of light intensity. An eye with central angiospastic retinopathy may read 20/20 on the illuminated chart but only 20/50 through the pinhole.

The pinhole has many instructive classroom applications. The muscae volitantes are most easily demonstrated by peering through a pinhole at the sky. While looking through the pinhole, if a pin is held close to the camera and moved slowly across the field of view, the movement seen will be in the contrary direction. With the object so high, the retina receives an erect image and consequently a reversed image is perceived through projection.

When one fixes the gaze through the pinhole on the 20/200 letter at 20 feet with an eye made artificially ametropic by plus or minus spheres, various interesting effects are observable. In the more refractive state (myopia) the movement of the pinhole from the eye causes the letter to diminish in size and become more distant; but with the less refractive condition (hypermetropia) the letter enlarges and appears nearer.

With eyes under cycloplegia the test is sensitive to 0.25D. If the eye is emmetropic or precisely corrected, the size and distance of the optotype remains apparently fixed. The particular change depends on whether the rays intercepted by the pinhole become closer to or farther from the far point of the eve examined.

In the previous experiments, if the pinhole is moved slightly in the frontal plane, there is an apparent motion of the distant target that corresponds to the pinhole movement in myopia and is against that movement in hypermetropia. The explanation is this: the crossing of the distant rays in myopia causes a reversal of movement on the retina which is reversed again by projection; in hypermetropia the uncrossed rays produce the opposite effect. A refinement of this test, applied to refraction by Holth in 1902, was termed by him kinescopy.

In subjective kinescopy as against objective skiascopy, the amplitude and rapidity of movement are directly instead of inversely proportional to the degree of ametropia; and the image is real, not apparent. In presbyopia, kinescopy can also determine the near point of accommodation. The observer moves the pinhole while regarding a suitable object such as the cross on the Lebensohn near-vision chart, held within near point. The pinhole motion causes an inverse movement of the cross which diminishes as the chart is moved away and first ceases when the punctum proximum is reached.

Stenopeic spectacles have a limited value for distance vision since they restrict the visual field and compel the wearer to move his head instead of his eyes. For this reason they are helpful in the after-care of detachment of the retina. The handicaps of stenopeic spectacles are of less hindrance in near vision and by their means a patient may sometimes be enabled to read who would be incapable otherwise.

As a reading aid a horizontal slit, if effective, is preferable to the pinhole aperture since it permits scanning movements. With Gill's adjustable stenopeic slit in the trial frame the optimum amplitude can be readily determined.

James E. Lebensohn.

## CORRESPONDENCE

SUDAN INTERIOR MISSION EYE HOSPITAL

Editor.

American Journal of Ophthalmology:

Located in Kano, North Nigeria, West Africa, is an eye hospital and clinic that is outstanding. According to statistics, there are 22,000,000 natives in Nigeria—a country reported to have the highest incidence of blindness in the world. There are only two ophthalmologists in the country—one a government man in Lagos on the coast and the other, an American, Dr. M. D. Hursh, in Kano, 700 miles inland. During the war there were a few military medical men that assisted, but none remained.

Dr. Hursh was inspired by Dr. A. D. Helser's book which discusses eye problems in Kano. He came to Nigeria in June, 1942, one of the few persons who were permitted to cross the ocean after war was declared.

Kano, during the war, was a training air base where 3,500 natives, 100 white officers, 300 R.A.F., and 300 A.T.C. personnel were stationed. Engines were repaired there. The Free French also had a unit of 100 or more men coming out of French West Africa.

The greatest problem in Nigeria, as far as proper care of eyes is concerned, is that it takes so long for patients to get to the hospital.

In the north, most inhabitants are Moslems; in the south, most are pagans and use their witch doctors until pain or trouble becomes extreme—then they make long trips on foot and it is often too late when they arrive. They will not take no for an answer when they do come and wait and wait around for help, often with an entire retinue. They insist that if an eye has been destroyed, the white man can put in a glass eye with which they can see! It has been impossible to convince them otherwise.

Another reason for not seeking medical aid is the rumor circulating in the "bush"

that a patient's eyes would be removed and goat's eyes inserted.

Only a third to a half of the cataract patients come back for surgery after the diagnosis has been made and cataract removal recommended. They either say "no" to surgery at the time, or they say they will talk it over, and set a date later and don't return, or they just don't return. By and large, however, most of them have confidence now in Dr. Hursh whose work is known in every village.

Training of African personnel, especially women, is very difficult. The natives interested in hospital work are usually from the southern part of Nigeria and it is necessary to employ interpreters who know several tribal languages. Six months are spent by the missionaries in learning the Hausa language.

Mr. S. N. Myers built the hospital with an African crew. He then learned the optical business and now operates a most efficient optical shop. The wage scale is interestingthe native (trained by Myers) optical shop employee gets 20 dollars a month, the nurses in training get 10 to 15 dollars a month and, after full training, 20 to 25 dollars a month. Their top pay is 28 dollars a month but they receive their uniforms and quarters and one month's holiday on pay with travel expenses. They work eight-hour day duty, 12-hour night duty, six days a week, with six hours on Sunday, Mrs. Hursh runs the blind school, takes care of records and hospital feeding problems. Their house is free but food and help have to come out of their very modest salary, as does transportation with gas at 60 cents a gallon.

The hospital building was started in August, 1942, and was dedicated in January, 1943. All of the furniture was made on the spot—even a slitlamp. After the war a Universal slitlamp was obtained plus army surplus equipment including metal beds.

A breakdown of case figures for 1948 shows: (1) The total number of patients blind in both eyes was 526: Trachoma, 173;

cataract, 132; leukoma, 57; atrophy bulbi, 44; optic atrophy, 15; pupil seclusion, 14; cataract and glaucoma, 14; keratitis, 5; choroiditis, 4; trachoma and glaucoma, 3; miscellaneous, 65. (2) Those blind in one eye totaled 742: Trachoma, 189; leukoma, 163; iritis and occlusion, 58; glaucoma, 51; atrophy bulbi, 46; injury, 28; ulcers, 17; miscellaneous, 190. (3) Differential diagnosis: Conjunctivitis, 2,851 (nontrachoma cases); miscellaneous, 1,102; trachoma, 974; refractions, 836; cataracts, 407; entropion, 292; iritis, 100; ulcers, 92; keratitis, 96; ectropion, 30.

The personnel of hospital (1949): One ophthalmologist, one optician, three American nurses, two American secretaries, 10 African nurses, two native secretaries, two native optical technicians, six native helpers (cook, janitor, etc.), two teachers in blind school (one African, one European).

A summary of work done in 1948: 5,630 out-patients, 26,646 treatments or daily visits (African native), 325 European patients (white), mainly refractions, 512 in-patients (298 men and 214 women), 470 major operations (152 entropion repairs, 142 cataract extractions, 126 miscellaneous), 19 minor operations.

The figures for the first four months of 1949 are nearly 50 percent above those for the same period of 1948.

(Signed) Hedwig S. Kuhn, Hammond, Indiana.

Education of the norwegian ophthalmologist

Editor,

American Journal of Ophthalmology:

Proposals to regulate the education of medical specialists in Norway were initiated by the Younger Union of Physicians in 1918, just a year after the inception of the American Board of Ophthalmology.

To be eligible for training in a specialty, a physician must have a medical background consisting of a general interneship of one year, and at least one year in general practice.

Preparation for ophthalmology requires three years of clinical experience, at least two of which must be in a Norwegian clinic of ophthalmology. Since 1936, credit is allowed for scientific contributions, laboratory work, and supervised private practice.

Final authorization is in the hands of a committee of four certified ophthalmologists, of which the professor of ophthalmology at the university is a member ex officio. There is no formal examination. A list of those certified in the various specialties is printed annually in the Yearbook of the Norwegian Union of Physicians. The certified specialist is permitted to announce his status in the telephone-directory listing and local newspapers; and this practice is general.

(Signed) G. W. Keyser, Oslo, Norway.

## BOOK REVIEWS

THE TRUTH ABOUT YOUR EYES. By Derrick Vail, M.D. New York, Farrar, Straus and Company, Inc., 1950. Clothbound, 180 pages, 6 figures, and index. Price: \$2.50.

Within the confines of a small book, Vail successfully deals with every aspect of the eye and vision of interest to the public "in a way that is informative without being alarming." Optometrical quacks are exposed yet recognition is accorded those qualified optometrists "who give the people ethical service in the proper sphere of optometry, which in the final analysis is the fitting of healthy eyes with proper glasses."

Although eye exercises of the Bates pattern are a ridiculous delusion, actual psychologic visual training is admittedly of some value, not as a substitute for glasses but as an added help. That the education of a child proceed unhandicapped by visual or functional defects is a responsibility of parents and teachers. Dyslexia can often be remedied by simply going back to the old-fashioned phonetic form of instruction. The layman—be he or she patient, parent, teacher, student, secretary, or nurse—will find in this work the meaning of 20/20 vision, suppression amblyopia, narrow- and wide-angle glaucoma, the prognosis of various operations, and a frank evaluation of all new "cures."

Tactful propaganda for the Eye-Bank is appropriately inserted among the broad implications of an efficient program for the prevention of blindness. Incidentally, ophthalmologists should demonstrate by example the courage of their convictions in this respect!

The eye care procurable by the American public today is most trustworthy since—
"Medical education in our country, so far free of political and government control, is the finest to be found anywhere."

The basic facts of ophthalmology, stated in this volume clearly and vividly, are well within the grasp of any literate layman.

James E. Lebensohn.

TRANSACTIONS OF THE AMERICAN OPH-THALMOLOGICAL SOCIETY. Philadelphia, Wm. F. Fell Co., 1949, volume 47, 776 pages.

At the 85th annual meeting of the American Ophthalmological Society, held on June 2, 3, and 4, 1949, the following scientific

papers were presented:

1. "Late fistulization of operative wounds: Diagnosis and treatment," Dr. John H. Dunnington and Dr. Ellen Regan. The early signs are profuse lacrimation, hypotony, and ciliary tenderness. Often a cystoid area is present. If leakage continues visual acuity may decrease and edema of the retina and optic nerve may occur. The fistula may be closed successfully by cauterizing the tract, suturing the tract edges, and covering the area with a sliding conjunctival flap.

2. "Simultaneous bilateral primary ocular malignant melanoma," Dr. Frederick C. Cordes and Dr. Robert D. Cook. The seventh case in the literature, confirmed by microscopic examination, is reported.

3. "Nevus flammeus associated with glau-

coma," Dr. Harold Joy. The case report is augmented by a discussion of the prevalent theories of the glaucomatous state.

4. "Goniotomy in the treatment of congenital glaucoma." Dr. Harold Scheie records the results obtained from goniotomy in the treatment of 16 eyes with congenital glaucoma. The tension was normalized in 11 eves by the Barkan procedure. Failure occurred only in the eyes in which the disease was far advanced before goniotomy.

5."Spontaneous cysts of the ciliary body simulating neoplasms," Dr. Algernon B. Reese. A common type of intra-epithelial cyst of the ciliary body is described and the clinical importance of the lesion is apparent because of the similarity to a neoplasm. The

cysts may produce glaucoma.

6."Sarcoid involving the orbit," Dr. F. N. Knapp and Dr. William V. Knoll, The differential diagnosis of sarcoid from uveitis requires a comprehensive study by the ophthalmologist, internist, roentgenologist, dermatologist, and pathologist. The etiology is undetermined.

7. "The psychology of the poor reader." Dr. William H. Crisp presents the problem of the psychology of vision as it is influenced by the recent educational methods of "flash" recognition of words and phrases in contrast to the old phonetic approach. Reading difficulties are not closely related to either the mental capacity of the child or to the amount of refractive error. The psychologic hindrances created by poor reading skill may be fatal to advanced progress. The difficulty must be corrected in the first year or so of schooling.

8. "Iris pigment flakes on posterior surface of cornea following cataract extraction." Dr. Walter S. Atkinson presents the first paper in the literature on this subject. Excessive iris trauma is apparently responsible for the flakes of pigment dislodged during cataract extraction. The flakes of pigment which may interfere with vision may be removed by irrigation of the anterior chamber.

9. "Lamellar keratoplasty: Technique and

results." Dr. Ramón Castroviejo describes the selection of cases, the technique of the operation, and presents his results. The method is safer than partial penetration keratoplasty but does not give as brilliant results. The illustrations are superb.

10. "Ocular conditions associated with idiopathic hyperlipemia." Dr. Edwin B. Dunphy reports the seventh case in the literature. The fundus, arterioles, and veins were cream colored against a milky background. There was an increase in the neutral fat, cholesterol, and phospholipids of the blood serum. The retinal vessels returned to the normal appearance when neutral fat dropped below 2,000 mg. percent, Xanthomatosis and lipid interstitial keratitis may be associated with idiopathic hyperlipemia.

11. "Oblique muscle surgery from the anatomical viewpoint." Dr. Walter F. Fink states: (1) The surgery on the superior oblique should be confined to the reflected tendon and its insertion and (2) the approach should be in the region of the insertion of the superior rectus muscle. An excellent anatomic description of the area is given. Surgery on the inferior oblique should be performed at the insertion without severing the lateral rectus muscle.

12. "Ocular fat embolism: A clinical and pathologic report." Dr. Arthur G. DeVoe reports a case with fundus drawings and a complete post-mortem examination. All organs revealed massive fat embolization of the capillaries and venules. The veins were engorged and fresh interstitial hemorrhages

were present.

13. "Retinitis punctata albescens." Dr. Arthur Bedell shows the photographic record of two cases-the first was under observation for 36 years, the second for 12 years. The small rounded lesions may be mistaken for drusen, Gunn's dots, vitreous reflexes, or white exudates.

14. "Cataract surgery routine in India." Dr. Raynold N. Berke.

15. "Experimental and clinical investigations on para-amino salicylic acid (PAS): Alone or in association with streptomycin in ocular tuberculosis." Dr. Trygve Gundersen and Professor G. B. Bietti present experimental and clinical results which justify the use of PAS and streptomycin in ocular tuberculosis in addition to the classical antituberculous means of therapy.

16. "Temporal arteritis as a cause of blindness: A review of literature and report of a case." Dr. Gordon M. Bruce reviews 84 cases in the literature; in 34 ocular involvement was noted; blindness in one or both eyes from retinal arterial obstruction occurred in 22 cases. The signs and symptoms of temporal arteritis forecast serious ocular trouble.

17. "Intra-ocular diktyoma and glioneuroma." Dr. F. Bruce Fralick and Helenor Campbell Wilder present the clinical and pathologic features of cases of congenital diktyoma, a locally malignant tumor of the nonpigmented epithelium of the ciliary body.

18. "How should we study primary glaucoma?" Dr. Eugene M. Blake points out the slow progress in uncovering the cause or causes of primary glaucoma. The following factors should be investigated: (1) The anatomic basis, (2) heredity, (3) psychogenic, (4) vascular, (5) the nervous system, (6) disturbances of metabolism, (7) allergy and others.

19. "Experimental and clinical use of aureomycin in herpes simplex." Dr. Alson E. Braley and R. C. Alexander find aureomycin has some effect upon the herpes virus in mice, rabbits, and in vitro. Its use clinically has been less effective.

20. "Tonometry; The variation of ocular rigidity in chronic glaucoma and an adaptation of the Souter tonometer." Dr. Searle B. Marlow advises the recording of the scale reading and the use of two weights. Variations in ocular rigidity in cases of glaucoma observed over a period of time were noted.

 "Cycloelectrolysis for glaucoma." Dr. Conrad Berens, Dr. L. Sheppard, and Dr. Arthur B. Duel describe cycloelectrolysis as a new operative technique for reducing intra-

ocular pressure in various types of glaucoma. It differs from perforating cyclodiathermy primarily in the type of current employed. The authors report their results on 65 eyes. In 23 eyes with primary glaucoma, the tension was controlled in 21; in nine eyes with secondary glaucoma following cataract extraction, five were controlled; in five eyes with acute glaucoma, all were controlled; in five eyes with hemorrhagic glaucoma, the tension was controlled in five eyes (100 percent); in hydrophthalmos, five eyes (100 percent) were controlled; in absolute glaucoma the tension was controlled in 57 percent. These results are enough to encourage others to try the method. Because of the slight reaction the operation may be performed as an office procedure.

The following theses for membership in the society are published:

"The role of hyperpyrexia in the treatment of ocular disease." Dr. Bennett Y. Alvis; "Roentgen therapy in corneal ulcers," Dr. J. Mason Baird; "The scleral resection (eyeball-shortening) operation," Dr. William E. Borley; "The clinical recognition and treatment of epithelization of the anterior chamber following cataract extraction," Dr. F. Phinizy Calhoun; "Migraine and its ocular manifestations," Dr. Hugh C. Donahue; "The role of vitreous in postoperative complications of intracapsular extractions," Dr. Willis S. Knighton; "The corneal nerves and their regeneration after surgery," Dr. L. Conner Moss; "Heterophoria and depth perception in aviation," Dr. John, V. V. Nicholls; "An experimental study of the possibility of transmitting syphilis by a corneal graft," Dr. M. Elliott Randolph; "Corneal edema," Dr. G. Victor Simpson; "Retrolental fibroplasia or ophthalmic dysplasia of premature infants," Dr. Arthur C. Unsworth.

This volume is exceptional both in the quality and quantity of the material presented. It is a preview of the further advances being made in ophthalmology and the associated fields of science.

William M. James.

OPHTHALMIC MEDICINE. By James Hamilton Doggart, M.A., M.D., F.R.C.S. Philadelphia, The Blakiston Company, 1949. 330 pages, 28 colored plates, 87 illustrations, index. Price: \$8.00.

The author has replaced Foster Moore in presenting a book on medical ophthalmology. He has been admirably successful in this task for his work is a beautifully illustrated manual of the subject that is suitable not only for the general physician for whom it is intended, but for all who are interested in ophthalmology.

The beauty of the book lies in the wealth of material compressed into such a short space without sacrifice of pertinent information. The author's style is pleasing and expresses his personality and philosophy on every page. It is a pleasant, scholarly per-

sonality that is reflected.

There are 35 chapters and, so far as could be determined, every subject from infectious diseases that affect the outer and inner eye to skin and glandular disorders is covered. The first four chapters are particularly valuable. They cover the subjects of history taking, symptoms, methods of examination, and physical signs. The book is highly recommended.

Derrick Vail.

COLOR PSYCHOLOGY AND COLOR THERAPY. By Faber Birren. New York, McGraw-Hill Book Company, 1950. 233 pages, illustrated, index, and bibliography. Price: \$4.50.

Here for the first time is an array of data on the history of color, with a complete review concerning its biologic, psychologic, and visual aspects. The book is divided into four parts.

It begins with a description of the historical aspects of color as it relates to superstition,

the story of mystics, charms, amulets, and aural and color healers. The second part deals with the biologic aspects of electromagnetic energy and the effects of visible and nonvisible rays upon plants, vertebrates, and invertebrates.

In the third section there is a description of the psychologic aspects of color therapy, with special emphasis on emotional reactions, the response of neurotics and psychotics, associ-

ations and analogies.

Part four concerns the effects of illumination, brightness, and color on the eye directly, a considerable proportion of the discussion being devoted to anomalies of seeing, color and night blindness, and the problem of eye strain as it is related to ideal seeing conditions.

The chapters on functional color and prescribing color in part four are very interesting. The term "functional color" applies to the application of hue where it is applied to aid visual acuity. The eye sees best in white, yellowish or yellow-green light, yellow being the color of highest visibility. Where a tinted background might be desired, yellow is suitable, but all coloring, as shown by Ferree Rand, is inferior to white if the printed characters are to be black.

Types of colors for industrial purposes are discussed in an interesting manner and, in the prescription of color, the effects of major hues are noted with the significance of color specifications in hospitals, schools, and factories.

The book is very well written and it contains a wealth of material which will interest certain medical practitioners, especially those engaged in industrial work. It is well to note, however, that there is and will continue to be a considerable difference of opinion as to the primary and secondary effects of color; a fair appraisal necessitates further research.

Irving Puntenney.

## ABSTRACT DEPARTMENT

## EDITED BY DR. F. HERBERT HAESSLER

Abstracts are classified under the divisions listed below. It must be remembered that any given paper may belong to several divisions of ophthalmology, although here it is mentioned only in one. Not all of the headings will necessarily be found in any one issue of the Journal.

## CLASSIFICATION

- 1. Anatomy, embryology, and comparative ophthalmology
- 2. General pathology, bacteriology, immunology 3. Vegetative physiology, biochemistry, pharma-
- cology, toxicology Physiologic optics, refraction, color vision
- 5. Diagnosis and therapy
- 6. Ocular motility
- Conjunctiva, cornea, sclera
- 8. Uvea, sympathetic disease, aqueous
- 9. Glaucoma and ocular tension

- 10. Crystalline lens
- Retina and vitreous
- 12. Optic nerve and chiasm 13. Neuro-ophthalmology
- Eyeball, orbit, sinuses
   Eyelids, lacrimal apparatus
- Tumors
- 17. Injuries
- 18 Systemic disease and parasites 19. Congenital deformities, heredity
- 20. Hygiene, sociology, education, and history

## ANATOMY, EMBRYOLOGY, AND COM-PARATIVE OPHTHALMOLOGY

Michaelson, I. C. The mode of development of the vascular system of the retina, with some observations on its significance for certain retinal diseases. Tr. Ophth. Soc. U. Kingdom 68:137-180, 1948.

The author demonstrates the vessel growth in the retina of man by a process of budding from pre-existing vessels. The formation of retinal capillaries is preeminently a function of retinal veins. Only the arterial afferents appear to originate from arteries. If the vein and artery are close to each other, growth takes place predominantly from the side of the vein that is away from the neighboring artery. The spread of the capillary growth towards an artery extends for only a certain distance and finally leaves, in the complete human eye, a well marked capillary-free space around the arteries similar to that found in other mammalian retinas such as those of cat, dog, rat and pig. These anatomical facts are clearly associated with each other and suggest the presence of a factor which affects the growth of retinal blood vessels. The factor is present in extra-vascular tissue of the retina, it is present in a gradient concentration such that it differs in arterial and venous neighborhoods and possibly is of a biochemical nature. Its action is on the retinal veins predominantly. The factor initiating capillary growth from the vein probably determines the distance to which the capillary growth will extend. Initiation and cessation depend on variation in concentration of the factor. This study of ontogeny shows that the bulk of the capillary system in the retina of man can be considered as part of the venous system. The arterial system is supracapillary.

The mode of development of the vessels elucidates the formation of new vessels under pathologic conditions such as diabetes, venous occlusion and Eales' disease. The developmental distinction between the arteries and arterioles on one side and the vein-capillary unit on the other has been shown to parallel the distinction between the pathologic patterns in hypertensive and diabetic retinopathies. (16 tables, 26 figures)

Beulah Cushman.

Mihályhegyi, G. The curvature of the anterior surface of the human eye. Ophthalmologica 119:344-363, June, 1950.

The configuration of the anterior surface of living human eyes was determined from molds made for the purpose of fitting contact lenses. Considerable difficulties were encountered and, for a good part, overcome. Most eyes examined proved thoroughly aspherical, with gross differences between the two halves of the same meridian. No regularity or definite pattern can be recognized in the data reported. The actual measurements are probably the most accurate ones available at this time.

Peter C. Kronfeld.

Sebruyns, M. Study with the electronic microscope of the ultra structure of pigment grains of the retinal epithelium. Ann. d'ocul. 183:393-399, May, 1950.

Under magnifications of 15,000 to 21,000 diameters, retinal pigment cells appear as elongated ovals of different lengths. At the extremity of each cell is a long filament which in life is apparently spirally coiled around the cell. Each cell is composed of hundreds of microgranules enclosed in a membranous sac. The structure, therefore, is a highly complex one. In this study the author employed fresh beef eyes in which the vitreous was removed and the pigment cells were detached with a fine curette. A four-percent chloramine T solution was used to increase the visibility of the pigment cells. The physicochemical changes involved in light exposure are not known.

Chas. A. Bahn.

2

GENERAL PATHOLOGY, BACTERIOLOGY, IMMUNOLOGY

Abt, K., and Brueckner, R. Spasm of the retinal arterioles in artificially hypertensive rats. Ophthalmologica 119:17-43, Jan., 1950.

The general plan of the paper is the ophthalmoscopic and microscopic study of the retinal vessels in experimental cardiovascular hypertensive disease produced in rats by wrapping a fairly tight cellulose acetate capsule around one kidney. This capsule compresses the kidney and, at the same time, causes a reactive inflammation. This procedure alone does not consistently cause hypertension. If the other kidney is extirpated 8 to 12 days later, a marked hypertensive disease sets in, the course and severity of which depends upon the tightness of the cellulose acetate capsule. If they are very tight the animal becomes uremic and dies within 60 days. With fairly loose capsules the animals remain in a state of chronic hypertension for a number of weeks, but finally also die of uremia.

Removal of the capsule after three months transforms the disease into a more chronic, less malignant hypertension. Sixty-eight rats treated in this manner were examined ophthalmoscopically (by the indirect method) and microscopically by removing their eyes, opening them equatorially and placing the whole retina on a slide under glycerine. The caliber of the retinal arterioles was found to be slightly increased in 2, normal in 14, slightly to moderately constricted in 30, markedly constricted in 21 and maximally constricted in 1 animal. Localized changes in the arteriolar caliber occurred eccentrically and, much more frequently, concentrically. The latter represented the most striking feature of the hypertensive fundus and occurred in the form of spindles, nodes, rosaries and combinations thereof. The irregularity of these constrictions suggested two possible interpretations: the contractile elements may be unequally distributed within the arteriolar wall or may respond unequally to the same stimulus. The latter interpretation seems to explain the variability of the constriction and dilation phenomena better than the former. The histologic findings will be reported later. The fundus picture is a reliable indicator of experimental renal hypertension.

Peter C. Kronfeld.

Cavara, V. Inflammations of the uvea due to filterable viruses. Boll, d'ocul. 29:3-28, Jan., 1950.

The author considers separately the uveal inflammations that unmistakably arise from filterable viruses and those in which the viral etiology is assumed but not proved; in the first group, iritis and iridocyclitis prevail, in the latter uveitis. Among the well-defined viruses are those of the exanthematic diseases (measles, German measles, scarlet fever, smallpox); the herpetic and herpetiform viruses (herpes febrilis, herpes zoster, chicken-pox, epidemic keratoconjunctivitis); other viruses of such diseases as influenza, mumps, Nicolas-Favre's disease, and dengue. The group with assumed virus etiology comprises uveomeningitis (the syndromes of Harada and Vogt-Koyanagi and sympathetic ophthalmia), systemic reticular endotheliosis (benign lymphogranulomatosis and malignant lymphogranulomatosis), Heerfordt's uveoparotid fever, possibly connected with Schaumann's disease; Behcet's syndrome, uveoarticular syndromes (acute articular arthritis: Still's disease. Reiter's disease). In the University Eve Clinic in Rome, extensive etiologic and therapeutic research has been performed: for the whole group, no specific treatment is available. (References)

K. W. Ascher.

DeVoe, A. G. Ocular fat embolism: a clinical and pathologic report. Arch. Ophth. 43:857-863, May, 1950.

Although there is no doubt that gross trauma is the most frequent causative factor, fat embolism has been found as a complication of burns, surgical manipulation of joints, therapeutic injection of oily substances, injection of paraffin into the orbit as a reparative procedure, and poisoning by ammonia and other alkalis. Fracture of one or more of the long bones is most often the chief traumatic lesion.

The supposed rarity of ocular embolism, then, is possibly attributable to several causes. Ophthalmoscopic examination is not likely to be requested unless cerebral changes are obvious and the cerebral form of the disease, with widespread dissemination of the globules, is uncommon. Fat may be present in the retinal vessels without detectable changes in the fundus. A review of the literature revealed that fat embolism of the human eye is not so rare as has been believed. A case is reported in which it was possible to sketch the fundus before death and later to secure a complete necropsy.

Ralph W. Danielson.

Didion, Hans. The anatomic changes of the eyeground in Niemann-Pick disease. Klin, Monatsbl. f. Augenh. 116:131-135, 1950.

The eyes of twins with Niemann-Pick disease were examined histologically. The characteristic grayish ring around the cherry-red spot in the fovea was noted at the age of 14 months and remained unchanged until death. Lipoid degeneration was found in all tissues, including the central nervous system. The eye findings in the twins were identical. The sclera and choroid were intact. The epithelial layer of the retina was normal. In the macular region the ganglion-cell layer was 5 mm. thick, the ganglion cells were swollen and round, the plasma of fine foamy structure, the nuclei pushed to the side and shrunken. The ganglion cells were not diminished in number. Polarizamicroscopy showed numerous doubly refracting crystals. The bipolar nerve cells in the inner zone of the inner nuclear layer, too, were of fine foamy structure. The rest of the retina beyond the macular region was normal. Neither the optic nerve nor the nerve-fiber layer showed signs of optic atrophy. The nerve sheath was rich in foam cells.

R. Grunfeld.

Francois, J., and Rabaey, M. Cytologic and bacteriologic study of the conjunctival secretion: the Pityrosporum ovale. Ann d'ocul. 183:378-392, May, 1950.

Pityrosporum ovale was identified in only two of 50 cases of blepharoconjunctivitis which were studied cytologically. In these cases the organism, which is 2 to 7 µ long and 1½ to 7 µ in breadth and oval or bottle-shaped was obtained almost in pure culture. The organism is not sensitive to biotics. In culture it was grown best on a medium containing 1 percent gelose with 1½ percent bleic acid. It was destroyed by nitrate of silver, 1 percent tetramine mercuric ointment and 1 percent salycylic ointment. The author believes the pityrosporum ovale to be pathogenic and not saprophytic.

Chas. A. Bahn.

Hansen, E. W. Allergy in ophthalmology. Tr. Am. Acad. Ophth. pp. 299-311, March-April, 1950.

Nearly every tissue in and about the eve is capable of becoming sensitized to one or more of a multitude of allergens. These include drugs such as penicillin, atropine, butyn and eserine, pollens, various foods, cosmetics, bacteria and even organ specific proteins like lens material and uveal pigment, A careful history is essential in detecting the culpable allergen, and in outlining a course of Supplementary bacteriologic therapy. studies and sensitivity tests, when indicated, verify the conclusions drawn from the history. Among the allergic conditions involving the lids and conjunctiva are phlyctenular disease, staphylococcus conjunctivitis, and vernal conjunctivitis. Cytologic examination with the finding of eosinophiles in the conjunctival secretion suggests allergy. The cornea and sclera may become involved when there is a sensitivity to tuberculoproteins and in congenital syphilis. Interstitial keratitis of congenital syphilis is an allergic reaction.

The uveal tract often becomes sensitive to tuberculoprotein, and to the toxins produced at foci of infection. Both the granulomatous and nongranulomatous types of uveitis, whether due to tuberculosis, syphilis or sympathetic ophthalmia are responses of an allergic nature. Cataract, glaucoma, retrobulbar neuritis and other intraocular conditions may on occasion be part of an allergic state.

Gustav C. Bahn.

Müller, Horst. Histologic examination of an eye in acute, fatal, methyl alcohol poisoning. Klin. Monatsbl. f. Augenh. 116:135-144, 1950.

A 27-year-old man died 18 hours after acute methyl alcohol poisoning. Histologic examination of the eye revealed massive exudation from the choriocapillaries. The edema formed multiple holes in the pigment epithelium over which the other retinal layers were detached and formed small steep folds. The pigment epithelium itself was torn off at places and was folded over itself. The retinal vessels, too, were changed by the toxin and showed increased permeability, perivascular edema, and edema of the whole nerve fiber layer.

R. Grunfeld.

Poleff, L. Culture of the trachoma bodies "in vitro" and in the developing chick embryo. Arch. d'opht. 10:202-211, 1950.

The author claims cultivation of the elementary and initial bodies of trachoma in tissue culture and in the yolk sac of the developing chick embryo. For tissue culture he employed tunica vaginalis of the guinea pig, embryo kidney of the rabbit, embryonic cornea of the chicken, adult human cornea, placenta, human hernia sac, and human iris tissue, and states that he obtained growth of the bodies in 25 of 41 experiments. It is to be noted that the observations were entirely morphologic and that the presence

of virus was not confirmed by monkey or human inoculation. The author stresses the need for human inoculations.

Phillips Thygeson.

Saebo, Johan, and Hagelsteen, Henrik. Clinical and bacteriologic examinations of eye lesions. Acta ophth. 27:517-536, 1949.

Twenty-five ocular injuries with intraocular foreign bodies were studied bacteriologically with the purpose of establishing the clinical value of such studies. Cultures were taken from the conjunctiva and the extracted foreign body; in cases which ended in enucleation the eyeball was punctured and a culture made from the vitreous. The enucleated eyeballs were examined histologically. A detailed clinical report of the 25 cases, as well as the laboratory studies, are reported. These cases date from the prepenicillin era.

Ray K. Daily.

Sheldon, J. M., Lovell, R. G., and Mathews, K. P. Immunologic aspects of allergy. Tr. Am. Acad. Ophth. pp. 277-282, March-April, 1950.

Histamine is now known to be a dominant factor in responses elicited by foreign protein in previously sensitized individuals, although other agents are also involved. Two types of allergic response are encountered, depending upon the reaction time of the response, and upon the manner in which the antigen and antibody are brought together. Immediate wheal reactions are induced by parenteral administration of the antigen in contrast to spontaneous reactions such as occur in asthma or hay fever. A blocking antibody is thought to be particularly important in the desensitization treatment of allergic states. Unlike the skin-sensitizing antibody, the blocking antibody is a heatstable protein which can be produced in nonallergic individuals, and which has no affinity for skin or mucous membranes. Attention is directed to the role of the

psychogenic factor and the relation of endocrine balances in allergic states. The pituitary-adrenal axis is becoming recognized as an important factor in the endocrine allergy equation. Many allergic conditions have been dramatically relieved by adrenocorticotropic hormone. The effects of puberty, menstruation, pregnancy, menopause, and other periods of endocrine turmoil are known to affect allergic conditions. Gustav C. Bahn.

3

VEGETATIVE PHYSIOLOGY, BIO-CHEMISTRY, PHARMACOLOGY, TOXICOLOGY

Amsler, Marc. (Bowman Lecture) New clinical aspects of the vegetative eye. Tr. Ophth. Soc. U. Kingdom 68:45-74, 1948.

The author distinguishes a morphological, a sensory and a vegetative eye. The first is the anatonic structure, the second an integrated unit of the functions of light, color, and form sense and binocular fusion, and the third the pattern of process by which the life of the organ is carried on so that the organ may carry out its visual function in the interest of the body as a whole.

To study the effects of the vegetative eye, detailed examination was made of 0.10 to 0.20 cc. of aqueous obtained in 2,500 anterior chamber punctures. One of the 8 to 10 drops available was used for the precipitation of the total protein by means of the Pandy reagent, one for cell counting, one for bacteriological culture in Rosenow's liquid medium, the fourth for study with the ultramicroscope with dark ground illumination, and the fifth and sixth were centrifuged, fixed and stained for the identification of the cellular elements. When desirable, further tests were made for sugar, chlorides and vitamins.

The ultramicroscopic study of the aqueous humor with dark ground illumi-

nation leads to the study of the aqueous as a biological whole, the liquid and the cells. The study of the aqueous after the intravenous injection of 2 ml. of 10 percent fluorescein sodium was also made. It was found in the anterior chamber after one to six minutes and came through the pupil. In pathologic conditions the excretion of the dye is always increased and disappears rapidly. There is no sharp distinction between iridocyclitis, diseases of the fundus, injuries to the eyeball or glaucoma simplex. The fluorescein test in general disease such as arterial hypertension is always increased as soon as the damage done to the capillaries gives rise to edema characteristic of malignant hypertension retinopathy.

In Kimmelstiel's syndrome (renal insufficiently plus diabetes) there is an enormously increased permeability. Increased permeability was also noted in general conditions which produce edema, such as obesity, hyperthyroidism, Addison's disease or allergic states. Histamine increases permeability. (27 figures)

Beulah Cushman.

Auricchio, Giacinto. Direct oxidation of glucose by the retina. Ann. di ottal. e clin. ocul. 76:52-61, Feb., 1950.

The ability of monoiodoacetate to inhibit completely retinal glycolysis in a concentration in which the oxidation of glucose is inhibited only in part, and the ability of the retina to oxidize gluconate and 2-ketogluconate lead Auricchio to the conclusion that in retinal tissue there exists some direct way (that is, not preceeded by glycolysis) of oxidizing glucose. This way probably involves successive oxidations and decarboxylations of the substrate, and employs not less than 25 percent of the total quantity of oxygen used by the retina for the oxidation of glucose. In his experimental work Auricchio used Warburg's manometric technique. (Charts and references)

Harry K. Messenger.

Azzolini, U., and Faldi, S. The tolerance for aureomycin of the aqueous and vitreous of rabbits. Giorn. ital. oftal. 3:24-26, Jan.-Feb., 1950.

The injection of 1.5 mg. of aureomycin into the anterior chamber of rabbits caused serious edema of the cornea, turbidity of the aqueous and hyperemia of the iris. All these lesions disappeared completely. The injection of 3.5 mg. of aureomycin into the vitreous is followed by its disorganization and lesions of the retina similar to those observed with other antibiotics. Vito La Rocca.

Azzolini, U., and Faldi, S. Chloromycetin tolerance in rabbits. Giorn. ital. oftal. 3:211-213, May-June, 1950.

The aqueous solution of chloromycetin in a concentration of 2.50 pro mille is well tolerated if injected subconjunctivally or into the anterior chamber of rabbits. In the vitreous 0.50 mg, brings about the disorganization of the framework.

Vito La Rocca.

Bailliart, P. The tonus of the retinal arterioles. Ophthalmologica 118:589-596, Oct.-Nov., 1949.

In very general terms Bailliart discusses the function of the retinal arterioles. Thanks to the tonus of the muscle in their walls, the rate and speed of circulation are regulated without visible changes in caliber. The vessels of the brain as well as of the retina are supplied with vasomotor nerve fibers. Examination of the retinal circulation in the living human eye is more revealing and simpler than laboratory studies on experimental animals. It is not sufficient to inspect the vessels and to measure their caliber. The very variable active resistance of the arteriolar wall can be estimated by determining the pressure in the retinal arterioles. The reader is referred to an important recent monograph on the subject of retinal blood pressures by Streiff and

Monnier (J. Springer, Vienna, 1946).

Peter C. Kronfeld.

Bailliart, P. Capillary permeability. Ann. d'ocul. 183:361-377, May, 1950.

Changes in capillary size and corresponding changes in capillary filterability are frequently dissociated, especially in degenerative diseases. The capillary bed is normally adapted both quantitatively and qualitatively to the specific needs of each organ and tissue. The complex mechanism which governs qualitative capillary function in both health and disease is not yet well understood. In most inflammatory diseases the prearterial and prevenous capillaries are dilated. Redness and corresponding increased permeability of a specific type results. In many diseases characterized by hormonal disturbances and disturbance of the metabolism of vitamins, the basic lesions are closely associated with an abnormal regulation in the capillary bed, and specific chemical substances emerge from, or enter into, the bloodstream. In oriental epidemic dropsy with glaucoma the causative vitamin B deficiency results in a capillary dysfunction characterized by the production of an edematous fluid which is relatively unfilterable through the cornea-scleral trabeculum. In vitamin C deficiency the intercellular substance of the capillary endothelium is primarily involved and exudation and hemorrhage result. In vitamin K deficiency capillary fragility is frequent and is an aggravating factor in numerous retinopathies and some glaucoma. The administration of vitamins C and P as an auxiliary treatment in primary glaucoma not normalized by miotics is logical. Sympathetic and parasympathetic vasomotor capillary control is an important factor in hormonal diseases but section of sympathetic nerves has not vielded conclusive data on which an explanation might be based. The orbital edema associated with exophthalmus in

hyperthyroidism is largely due to quantitative and qualitative abnormalities of capillary permeability, the exact mechanism of which is not thoroughly understood. The favorable results which have followed the administration of ACTH in numerous inflammatory diseases is apparently due to increased oxidization and closely associated with capillary function. In diabetes, degenerative lesions, especially of the prevenous capillary bed, cause the microaneurism observed in the retina and elsewhere. Small doses of insulin increase capillary permeability, large doses decrease it. Toxic substances such as are formed in some degenerative renal diseases are closely associated with altered capillary permeability both in the kidney and in the eye. Degenerative changes in the capillary bed with decreased permeability are also a prominent factor in some forms of atherosclerosis with and without Chas. A. Bahn. hypertension.

Balavoine, C., and Vuataz, N. Microdeterminations of the protein-nitrogen of the aqueous. Ophthalmologica 118:356-368, Oct.-Nov., 1949.

The authors describe a carefully worked-out micromethod for determining the protein content of the aqueous. The substances containing nonprotein-nitrogen are removed by dialyzation; in the residue the proteins are converted into ammonium salts by a Kjeldahl procedure, using selenium as a catalyzer. For the aqueous of rabbits the authors obtain protein contents varying from 0.019 to 0.070 mg. percent. Peter C. Kronfeld.

De Bernardinis, E. Metabolism of the cornea and lens. Giorn. ital. oftal. 2:350-367, Sept.-Oct., 1949.

The author reports his own experiments on the respiration and anaerobic glycolysis of the cornea and lens with the method of Warburg in normal rats and others deprived of tryptophane. There is a lessening of the amount of oxygen in the cornea, of the anaerobic glycolysis of the cornea, and of the amount of oxygen taken in the mature cataract; an early decrease of the anaerobic glycolysis of the lens; a decrease of the glucose content of the lens in incipient cataract; and an increase of the intralenticular intake of glucose and of the permeability of the lens capsule.

Vito La Rocca.

Boros, B., Méhes, G., and Arató, M. Biologic features of placental extract. Szemészet 1:10-18, 1950.

One hundred cc. of the aqueous extract contains: dry substance, 20 mg., inorganic salts, 4.8 mg., organic ingredients, 15.8 mg., potassium 2.6 mg., and calcium 2.2 mg. The pH of the solution ranges from 5.5 to 5.8. On desiccation in vacuum marked foam is produced, probably as a result of colloidal substances. The solution, isotonic and isoionic at a pH 7.2 was applied to frog's heart prepared by Straub's method. If 0.2 cc. or more was applied the inotropic and tonotropic effect was markedly positive. The effect occurred gradually rather than suddenly. Finally, the effect of the solution on atropinized bowel was studied in comparison with histamin. It could be inferred from these experiments that 1 cc. of the solution contained 0.0001 to 0.005 microgram of histamin-like substances.

Gyula Lugossy.

Brolin, S. E., and Krakau, T. Spectrophotometric investigations on the fluorescence of the ocular lens with changed metabolism in rats with galactose. Acta ophth. 27:291-301, 1949.

Experimental galactose cataracts in 22 rats were compared with 19 normal controls. Brolin's method was used for measuring the distribution of the spectral intensity objectively and microscopic observation for differentiating the type of fluorescence. The data, reported in detail,

show a probable increase in the fluorescence of the cortex of the cataractous lenses. The changes in fluorescence appear early and could be used for differentiating different forms of cataract at an early stage.

Ray K. Daily.

Buschke, Wilhelm. Experimental studies of the pathophysiology of the corneal epithelium. Ophthalmologica 118:407-439, Oct.-Nov., 1949.

This paper is essentially a concentrated review of a major portion of the experimental work on the healing of corneal wounds which was done by the author with the help of various associates at the Wilmer Institute between 1939 and 1947. Most American readers, though familiar with the essential experimental findings, will find this review valuable because of its unifying "dove-tailing" character. Quantitative methods were developed for the study of the processes entailed in the healing of corneal wounds. The primary healing process was found to consist of cell migration without cell division. This migration occurs in a manner that expresses a tendency toward cellular continuity and suggests the effect of surface forces. Besides, metabolic processes are entailed in this epithelial migration. Low temperature, anoxia and various enzyme poisons inhibit the migration. Mitotic activity proved to be a secondary process in wound healing. The effect of various factors upon the mitotic process was studied. Peter C. Kronfeld.

Campbell, F. W., and Ferguson, I. D. The role of ascorbic acid in corneal vascularization. Brit. J. Ophth. 34:329-334, June, 1950.

Increased incidence of vascularization in wound healing occurred in ascorbic acid-deficient guinea pigs compared to a control group. There was no significant difference in the healing time in the two groups. The onset of vascularization, the

time of maximum extent, and the time of disappearance all tended to be delayed in the scorbutic group. Ascorbic acid is necessary for formation of collagenous tissue in the repair of wounds in the cornea, and these injuries apparently unmasked a deficiency not otherwise apparent. In the formation of new collagen the metabolic demands apparently cannot be properly met in a state of scurvy.

Orwyn H. Ellis.

Cassady, J. V., Thompson, J. M., and Pope, J. L. Influence of certain mydriatics on the ascorbic acid content of the aqueous humor. Arch. Ophth. 43:813-817, May, 1950.

The authors used young rabbits for their experimental studies and conclude that in the rabbit eye the instillation of atropine does not affect the quantity of ascorbic acid present in either the reduced or oxidized form. The admonition to avoid the use of atropine-like drugs before and after operation, as an inciter of hyphema, at least with respect to their ascorbic acid reducing effect, seems unwarranted.

E. J. Swets.

Davson, H., and Thomassen, T. L. The effect of intravenous infusion of hypertonic saline on the intra-ocular pressure. Brit. J. Ophth. 34:355-359, June, 1950.

The blood concentration of NaCl was gradually and continuously raised by intravenous drip and the intraocular pressure recorded. In general, hypertonic saline solution produced a slow decline of intraocular pressure which gradually decreased, and the pressure became nearly constant. Analysis showed a considerable excess sodium in the blood over the aqueous. After the infusion was stopped the intraocular pressure showed no sign of returning to normal even when followed for a long time. Although the intraocular pressure can be modified by purely osmotic means, the final result is deter-

mined by a balance of the osmotic withdrawal of fluid and its secretory formation. Too great a fluid loss is thought to be compensated for by increased rate of formation. There is a tendency for the concentration of sodium in blood and aqueous to become equal by withdrawal of water from the aqueous.

Orwyn H. Ellis.

Ditrói, G., Karády, I., and Skultéty, S. Experimental contributions to the mechanism of Filatov's therapy. Szemészet 1:5-9, 1950.

By applying Jancso's india ink method to rats it has been demonstrated that Filatov's extract of placenta leads to general histamin release both at the site of application and in the whole organism if greater doses are given hypodermically. Thus Filatov's therapy acts through two mechanisms: the administration of biogenous stimulants which represents an immediate help to the defensive regenerative processes and the release of histamin which gives rise to defensive and reparative processes. Gyula Lugossy.

Dorello, Ugo. Opsonic power in the aqueous. Giorn. ital. oftal. 3:214-221, May-June, 1950.

Opsonic power is absent from the aqueous first extracted from a ram and is only moderate in the second aqueous and in the blood serum. It is clearly inferior to that in man, where the normal aqueous has no opsonic power, but the secondary has some opsonic power, though less than the blood serum.

Vito La Rocca.

Esente, I., and Petronio, G. Experimental "crysosis" of the bulbus with large doses of a gold compound. Giorn. ital. oftal. 3:133-145, March-April, 1950.

By biomicroscopic and histochemical means the authors demonstrated the presence of gold in the eyes of rabbits which had been given 5 gr. of Crisalbina, a gold compound. Metallic gold was deposited in decreasing quantity in the muscles, in the corneoscleral zone, in the ciliary processes, in the iris, choroid, sclera and in the sheaths of the optic nerve. In a single rabbit after a larger dose the walls of the central retinal artery near the optic disc were also infiltrated, but no gold was found in the optic nerve, the retina or the lens. Mesenchimal tissue receives the greatest deposit of metallic gold.

Vito La Rocca.

Fischer, F. P. Fluid and interfacial films in ophthalmology. Ophthalmologica 118:335-344, Oct.-Nov., 1949.

In the words of the author, who has since died, the purpose of the paper is to define fields for further scientific investigation rather than to state established facts. The specific topic is the occurrence in the eye of fluid films and interfacial films which exhibit the physicochemical phenomena characteristic of such structures. One such film is the precorneal film of which Fischer has made a special study by means of his method of photographing the corneal mirror reflections. In vitamin A deficiencies and in keratoconjunctivitis sicca the precorneal film undergoes characteristic changes. Another fluid film is a thin immobile layer of aqueous contiguous to the corneal endothelium. As long as this aqueous film is complete, no precipitates can form. If the endothelium is damaged, the damaged portion becomes unwettable, the fluid film becomes incomplete and precipitates form.

Where vitreous borders upon the lens, the aqueous, or on the retina, it forms a true, organized border layer not just a fluid film. The ciliary epithelium probably permits some but, in principle, restrains the fluid exchange between the uvea and the chambers of the eye. The visual purple in the outer limbs of the rods is arranged in definite well organized layers which alternate with purple-free protein layers.

Peter C. Kronfeld.

Fritz, A. Progress in the study of retinal circulation. Ophthalmologica 118: 597-606, Oct.-Nov., 1949.

For over 20 years the author has been very actively engaged in studies of the hemodynamics of the human retina. His methods, which are largely based on Bailliart's ophthalmodynamometry, as well as his original observations and measurements, are recorded in the French and Belgian literature. In the article under review Fritz describes briefly the important steps or phases in his own work. He describes his method of determining the capillary pressure in the retina which is based on the observation of a sudden change in the color of the disc that occurs as the ophthalmodynamometrically raised ocular tension reaches a certain level.

Fritz considers the pressure level at which the most proximal portion of the central retinal vein (on the disc) collapses as the most reliable criterion of the venous pressure in the retina. A number of practical applications of these studies are quoted. The outcome of an obstruction of the central retinal vein can, to a certain extent, be predicted on the basis of the venous pressure findings. If the latter is very high, hemorrhagic glaucoma invariably ensues. If the venous pressure is lower than 50 grams (Bailliart's dynamometric units) there is good possibility of a cure.

Peter C. Kronfeld.

Gerber, H. Experiences with the ophthalmic ointment Irgafen. Ann. di ottal. e clin. ocul. 76:62-65, Feb., 1950.

Irgafen, an ophthalmic ointment put out by Geigy of Basel, consists of dimethylbenzoyl-sulfanilamide and dimethylacroyl-sulfanilamide (total concentration 15 percent) in a base which diffuses rapidly and mixes perfectly with the lacrimal fluid. Excellent results are obtained in blepharitis, blepharoconjunctivitis, conjunctivitis of bacterial origin, marginal ulcers of the cornea, and epidemic superficial punctate keratitis, and in preventing infection after injuries of the cornea. Irgafen is exceedingly well tolerated, causes no discomfort, and has no undesirable side effects. Gerber considers it to be equal to the best medicaments of its kind now in use and in many cases superior to any of them. (References)

Harry K. Messenger.

Giardini, Aniceto. Effects of alcohol on fusion. Giorn. ital. oftal. 2:446-451, Nov.-Dec., 1949.

Giardini studied the behavior of amplitude of fusion in adduction in 12 subjects after the administration of alcohol in doses of 1 gr. per kg. of body weight. The alcohol brought about a net lessening of the ability to focus 10 minutes after the ingestion of alcohol, which decreased rapidly after 30 minutes.

Vito La Rocca.

Goldmann, H. Fluorescein in the anterior chamber of man. Ophthalmologica 119:65-95, Feb., 1950.

The author reports the results of a systematic study of the factors that govern the fluorescein concentration in the aqueous after intravenous administration of this substance in man and rabbits. Such a quantitative study required, on the one hand, a method for the determination of the freely diffusible portion of the fluorescein present in the blood, and, on the other hand, a method for the determination of the fluorescein concentration of the aqueous in vivo and in situ. The first problem was solved by an intricate ultrafiltration technique, applicable to fresh uncitrated blood. Five cc. of blood vielded about 50 to 70 mg, of ultrafiltrate, the fluorescence of which could be determined accurately. The other problem, the measurement of the fluorescein concentration in the acqueous, was solved by a colorimetric method in which the darkadapted eve of the examiner compares,

by means of the biomicroscope, the fluorescence within the chamber with the fluorescence of a standard source.

In the typical experiment 4 cc. of sterile 10-percent sodium fluorescein was injected intravenously. During the next four hours four blood samples were drawn and examined for their content of diffusible fluorescein. The fluorescence of the chamber contents was measured about eight times during the same period. The maximum in the aqueous was reached about 100 minutes after the injection and then the fluorescence of the aqueous was only one-tenth of that of the blood. No diffusional equilibrium between blood and aqueous was reached at any time, which is probably the most important fact established by this study.

The author worked out an equation based on the assumptions of 1. free diffusion of fluorescein into and out of the chambers of the eye and 2. a certain amount of transfer of water into the posterior chamber. The constants in this equation were derived from the experimental data. This equation permitted an estimation of the volume of flow per minute through the anterior chamber. The result, 1.1 percent of the chamber contents or roughly 2 cu. mm. per minute,

Henderson, J. W., and Prough, W. A. Influence of age and sex on flow of tears. Arch. Ophth. 43:224-231, Feb., 1950.

is strikingly close to that obtained by

Peter C. Kronfeld.

other methods.

Statistical data are presented on the flow of tears in normal eyes as measured by a modified Schirmer test. Increase in age yields a slight corresponding decrease in the flow of tears. Males in the 15 to 29 age group showed an apparent normal of 20 mm. in five minutes and females in this group approximately 13 mm. After 60 years of age women showed a slightly smaller flow of tears than normal men of the same age.

John C. Long.

Krakau, C. E. T. The aqueous humor and histamine. Acta ophth. 27:259-262, 1949.

Diagrams of the contractions produced in the isolated gut of the guinea pig by aqueous aspirated from a rabbit's eye are unlike those produced by histamine but resemble those produced by adrenaline compounds. Ray K. Daily.

Marg, E., and Morgan, M. W., Jr. The pupillary fusion reflex. Arch. Ophth. 43:871-878, May, 1950.

In 1936 Schubert and Burian published their discovery of the pupillary fusion reflex which was defined as a dilatation of the pupil with a disruption of fusion and, conversely, a constriction of the pupil with its resumption. This reflex was said to be lasting, not evanescent. No further report has been published on the subject. After analysing data obtained for 15 subjects, the authors conclude that statistical analysis with use of the method of analysis of variance fails to show any such reflex. It would appear that the reflex originally discovered was an artefact which may easily occur without strict control of accommodation, illumination and convergence. Ralph W. Danielson.

Miratynska-Ernestowa, Elzbieta. Selagine as a substitute for pilocarpine and eserine, Klinika Oczna 18:437-449, 1948.

The author presents the results of tests with a new alkaloid called selagine obtained from lycopodium selago. The action is similar to pilocarpine. It acts by stimulating the endings of parasympathetic nerves. Selagine hydrochloride 1 percent was tested on 10 normal persons and 25 glaucomatous patients. The drug caused contraction of the pupil and decreased tension, but no local irritation or other secondary effect.

Sylvan Brandon.

Palm, Erik. The exchange of phosphate between the blood and the eye, studied with the aid of radio-autographs. Acta ophth. 27:267-274, 1949.

In a study of phosphate metabolism in the eye, 32P was injected intraperitoneally into guinea pigs. The animals were killed 1 to 11/2 hours after the injection, the eves were frozen and sectioned. The sections were placed in contact with photographic film which was darkened by the radioactive material. The pictures thus obtained gave an indication of the distribution of the newly injected phosphate in the eye. The radio-autographs confirm the belief that the main exchange between the blood and the avascular ocular media takes place through the vascular region in the anterior parts of the uvea. Here the radioactive substance enters the eye, and the parts of the vitreous and the aqueous lying closest to this region have a high radio-activity. The radio-autographs of the lens confirm the author's former conclusions, that in experiments of short duration the radio-active substance does not penetrate into the lens, and is found only in a thin layer on the surface. (4 figures) Ray K. Daily.

Palm, Erik. The phosphate content of the vitreous body. Acta ophth. 27:553-561, 1949.

A laboratory study of the inorganic phosphate content of the vitreous body and aqueous humor in eyes of the rabbit, the ox and the horse shows that the phosphate content of the vitreous is only one third that of the aqueous. It is higher in the most anterior portion of the vitreous which borders on the ciliary body. Reasons for this difference in the phosphate content are discussed, and it is suggested that the phosphates, like glucose, leave the vitreous by a phosphorylation.

Ray K. Daily.

Persichetti, Carlo. The effects of several myotics after anesthetic block of the ciliary ganglion. Giorn. ital. oftal. 2:452-476, Nov.-Dec., 1949.

The author discusses the results of tests made in man with various miotics after an anesthetic block of the ciliary ganglion by a retrobulbar injection of 2-percent novocaine solution. There was greater sensitivity of the pupil to pilocarpine and carbamino-ethyl-choline, a lack of response to eserine, which causes myosis only if it is associated with acetylcholine, and a delayed reaction to prostigmin. It is assumed that the retrobulbar novocaine causes a temporary reduction in the production of acetylcholine at the myoneural junction.

Vito La Rocca.

deRoetth, Andrew., Jr. Choline acetylase activity in ocular tissues. Arch. Ophth. 43:849-852, May, 1950.

Choline acetylase, the enzyme responsible for the synthesis of acetylcholine, was found in measurable amounts in the iris, ciliary body and retina of the cat and rabbit. The relative rates of choline acetylase activity were approximately proportional to the relative rates of cholinesterase activity found in these tissues.

Ralph W. Danielson.

Schaeffer, A. J., and Murray, J. D. Tryptophan determination in cataracts due to deficiency or delayed supplementation of tryptophan. Arch. Ophth. 43:202-216, Feb., 1950.

The development of cataract in experimental animals after protein depletion may be the result of disturbed protein synthesis because of the absence of one or more amino acids. Certain amino acids may have a specific role in the metabolism of the lens. The experimental work presented shows that in rats cataract develops despite delayed supplementation of large quantities of tryptophan. Prevention of cataract is accomplished only when all the essential amino acids are fed simultaneously. It is concluded that the synthesis of a protein molecule by the body is accomplished adequately

only in the simultaneous presence of all the essential amino acids; certain individual amino acids do not have a specific role in the metabolism of the lens.

John C. Long.

Scuderi, G. The permeability of the cornea to mydriatics. Atti d. 37 Congresso Soc. oftal. ital. 10:301-308, 1948.

In order to disprove the theory (Nakamura) that the corneal epithelium must be damaged before a drug can be absorbed through the cornea, various mydriatics in an isotonic and buffered solution were instilled into one eye of the patient. Both eyes were then carefully examined with the slitlamp. Lesions of the epithelium were only seen when a relatively high concentration of the mydriatic was used. For the common concentrations a lesion of the corneal epithelium is not necessary for corneal absorption. (References)

Frederick C. Blodi.

Scuderi, G., and Bonaccorsi, A. The permeability of the corneal endothelium to vital stains. Atti d. 37 Congresso Soc. oftal. ital. 10:309-316, 1948.

Various dyes were injected into the anterior chamber of guinea pigs and the eyes were studied with the slitlamp and histologically. The endothelium was found to have a selective permeability depending on the chemical properties of the dye. (References) Frederick C. Blodi.

Simonelli, Mario. Experimental study of the toxicity of vitamin K. Giorn. ital. oftal. 3:183-187, May-June, 1950.

The chemical affinity between vitamin K and naphthaline, which produces cataract, suggested this study of the toxic manisfestations of overdosage of vitamin K. The bulbus can remain undamaged except for a light hyperemia of the uveal vessels. There is a general toxic phase with heavy degenerative lesions of some internal organs, such as the liver, kidney

and suprarenal gland, which caused death. Vito La Rocca.

Simonelli, Mario. Permeability of the hemato-ophthalmic barrier. Giorn. ital. oftal. 2:329-334, Sept.-Oct., 1949.

With the use of fluorescein according to the method of Amsler and Huber the author observed variations in ciliary permeability in 20 normal subjects injected with vitamin K. In more than one half of them injection of this vitamin caused a slight lessening of permeability. If the injection is given intravenously, there is a transitory but very noticeable increase of permeability within one hour following the injection. This might be attributed to a capillarotropic reaction to vitamin K. It is wise to avoid intravenous injections of vitamins for therapeutic purposes.

Vito La Rocca.

Simonelli, M. The permeability of the blood-aqueous barrier. Atti d. 37 Congresso Soc. oftal. ital. 10:324, 1948.

Of all the vitamins only ascorbic acid influenced the blood aqueous barrier. It consistently increased the permeability. Increased permeability was also found in eves with detached retina.

Frederick C. Blodi.

Straub, Wolfgang. The treatment of serpentic ulcer with supronalum ointment. Klin. Monatsbl. f. Augenh. 116:187-191. 1950.

The author successfully treated 24 cases of serpiginous ulcer with local applications of 5-percent supronalum ointment, Supronalum is a combination of two sulfa drugs: methyldebenal and marbadal. Methyldebenal has the same property as any other sulfonamide. It binds and excludes paraaminobenzoic acid, an important bacterial ferment. Marbadal has a strong affinity for anaerobic bacteria, a peculiarity which is not shared by other sulfa drugs.

R. Grunfeld.

Süllmann, H., and Payot, P. Histochemical demonstration of alkaline phosphatase in the cornea. Ophthalmologica 118:345-355, Oct.-Nov., 1949.

The demonstration of enzymes by histochemical methods is an important method in the study of intermediary tissue metabolism. Phosphatases are enzymes that split phosphoric acid esters into their two components. The corneal epithelium of rats, rabbits and cattle was found to contain such phosphatases.

Peter C. Kronfeld.

Vancea, P., and Marculescu, C. Influence of implants of preserved tissue (method of Filatov) on the elemination of NaCl through the tears. Arch. d'opht. 10:212-216, 1950.

A study of the variations of NaCl in the tears after implants of preserved skin according to Filatov's method showed that there was an initial slight rise in NaCl content followed by a pronounced and prolonged drop. The authors consider that these variations might be due to acetylcholine liberated under the biologic stimulus of the implant and suggest that NaCl measurements might be of value as an objective method of estimating the biologic activity of the implants.

Phillips Thygeson.

Weekers, R., and Prijot, E. Experimental studies of the function of aqueous veins. Ophthalmologica 119:321-335, June, 1950.

The discovery of biomicroscopically visible aqueous veins in the common laboratory animals (Am. J. Ophth. 30: 186, 1947) has given new impetus to the investigation of the function of the drainage channels in the chamber angle. The typical appearance of aqueous veins in the rabbit is described. Their direct connection with the contents of the anterior chamber was demonstrated in experiments in which the aqueous was aspirated

and replaced with India ink. If the pressure in the anterior chamber was then raised, by means of a saline reservoir, to 20 mm. Hg, one could within one minute observe the entrance of black fluid into the aqueous veins. During such experiments the presence of extensive anastomoses and collaterals in the epibulbar vascular plexuses was established. Experimental variations of the pressure in the anterior chamber produced by raising or lowering the saline reservoir, produced characteristic changes in the appearance of the aqueous veins. If the intraocular pressure was lowered below 15 mm. Hg. all aqueous veins filled with blood. This phenomenon explained the entrance of blood into the canal of Schlemm observed by Kronfeld, McGarry and Smith (Arch. Ophth. 29:685, 1943). Clear fluid entered the aqueous and laminated veins if the intraocular pressure was raised to 20 or 25 mm. Hg. Ocular hypertension brought out the aqueous veins very clearly and, at times, revealed aqueousfilled channels which had been entirely invisible at normal tension levels.

In order to further study their function the author performed a surgical procedure intended to destroy all aqueous veins. This consisted of 1, undermining and section at the limbus of the bulbar conjunctiva, 2. coagulation by means of a high frequency current of all superficial epibulbar vessels back to about 4 mm, from the limbus and 3, section of all extrinsic ocular muscles at their bulbar insertions. After this procedure the ocular tension rose for about two hours and then dropped to a level of mild hypotony. The duration of this hypotony is not stated. During the latter the rate of entrance into the anterior chamber of intravenously administered fluorescein as well as the rate of outflow of the same substance from the anterior chamber was greater than in normal unoperated control eyes, Another important observation was the

occurrence of a considerable drop in tension in eyes operated upon by the aforementioned technique under the influence of external pressure.

The authors interpret the accelerated fluorescein transfer and the hypotony of the operated eyes as signs of uveal vasodilatation caused by the operative trauma. These experimental studies demonstrate that the canal of Schlemm and the aqueous veins are not the only outflow channels for the intraocular fluid and underline the importance of fluid transfer across the uveal capillary wall.

Peter C. Kronfeld.

Woodin, A. M. Hyaluronidase as a spreading factor in the cornea. Brit. J. Ophth. 34:375-379, June, 1950.

In the experiments conducted, hyaluronidase from several sources was found to be inactive as a spreading factor of the corneal mucopolysaccharides in situ within twenty-four hours. The results were similar when the cornea was waterswollen or collagenase-treated or untreated. The first two groups showed a significant increase in diffusion rate. The presence of hyaluronidase in pneumococcal filtrates would explain the spreading action of a pneumococcal infection.

Orwyn H. Ellis.

## 4

PHYSIOLOGIC OPTICS, REFRACTION, COLOR VISION

Allen, Frank. The neural oscillatory effect in color vision. Acta ophth. 27:599-619, 1949.

This investigation consisted of experiments in color vision, which might establish the neural oscillatory effect as a fundamental principle of neurology. Two graphs for the critical frequency of flicker of color for the whole spectrum were obtained; one for the right eye in daylight adaptation, and the other for the same eye adapted to one of the selected colors

alone, or when it was under the influence of the color adaptation of the left eye. Any difference between the plotted graphs could be attributed to the effect of the color adaptation. In this way the influence of adaptation to a single color on the perception of all parts of the spectrum could be easily ascertained. The equipment, method and data are described in detail. On the basis of former investigations and of this one the author unifies the Young and Hering theories of color vision into a single theory, the Young-Hering theory. The threefold nature of color stimulation combined with its twofold power of depressing one or two primary sensations and enhancing the complimentary sensation is a fundamental tenet of both theories. The sensation for white is not simple as in the Hering theory but is compounded of equal stimulation of the three primary sensations. The author conceives the retina as a receptor-integrator organ where, aside from photo-reception, many other processes usually associated with the central nervous system such as selection, facilitation, inhibition, summation of excitation, take place. The forwarding of the excitations which arise in the photoreceptors to the brain is, therefore, not a simple mechanical transmission, but an elaborate nervous process. The author finds in the complex visual apparatus nervous mechanisms adequate to explain the phenomena of the neural oscillatory effect exhibited in the experiments. Ray K. Daily.

Arbenz, Jean. The effect of drugs on after-images. Ophthalmologica 118:321-334, Oct.-Nov., 1949.

The usual miotics, mydriatics and vasodilators have no definite effect upon the course or intensity of after-images.

Peter C. Kronfeld.

Best, F. Optic agnosia, Klin. Monatsbl. f. Augenh. 116:14-18, 1950.

A case history is presented in which mind blindness developed at a late stage, four months after trauma in the occipital region. The patient had left-sided hemianopia. The visual fields were normal on the right side, but the visual cortex must have had been damaged too, for the visual acuity was reduced to 20/80 in the right eve and to 20/50 in the left. Furthermore, the patient was unable to recognize pictures and could not read the Stilling tables although he had good color sense. He was unable to localize objects in space. His egocentric localization was gravely disturbed and he could not remember the connection of two objects seen successively. It is evident that damage of higher optic functions resulted in optic agnosia. In the physiologic sense, the act of vision is built up at different levels and for different levels of vision special cortex areas and ganglion cells may serve, which mutually influence each other and become coordinated. Optic-spatial agnosia depends upon a lesion in the area between the calcarine and parietal lobe, optic-object agnosia on lesions extending from the calcarine to the temporal lobe. Within these centers are subcenters for alexia and agraphia. The sense for simple form is localized in the vicinity of the calcarine at the posterior occipital pole. R. Grunfeld.

Boehm, G. The entoptic phenomenon of blue arcs. Ophthalmologica 118:276-304, Oct.-Nov., 1949.

The extensive literature is critically reviewed. Most of the publications deal with the phenomenon of blue arcs as it is observed by individuals with normal visual functions. The author has studied the phenomenon in defective human visual systems, namely in hemeralopes and complete achromates. A simple apparatus for the elicitation of the phenomenon is described. Five out of six individuals with congenital hereditary night-blindness

could definitely see the entoptic phenomenon of blue arcs, but were unable to perceive actual blue arcs of the same or greater brightness, produced by projecting such arcs on a dark background. Two individuals with total congenital colorblindness observed and clearly described the entoptic phenomenon. From these observations the author concludes that the entoptic phenomenon of blue arcs is not dependent upon the presence of functioning cones and is not caused by bioluminescence of some of the stimulated papillo-macular nerve fibers (as had been assumed by some authors). The most plausible explanation of the blue arcs is furnished by the action current theory according to which the action currents passing through the papillo-macular fibers give rise to secondary stimulation of other, not primarily stimulated, cellular retinal elements. (77 references)

Peter C. Kronfeld.

Brandenburg, K. C. Ultraviolet effects on night vision. Ann. West Med. and Surg. 4:302, June, 1950.

Exposure to the invisible ultraviolet portion of the spectrum may be followed by a deterioration of dark adaptation and visual discrimination of at least 20 percent. These ultraviolet effects may persist as long as two hours after the eye is exposed to the unfiltered radiation from a television screen, fluorescent illumination or bright daylight. This may be a factor in the higher incidence of traffic accidents at dusk. Certain types of glass used as spectacle lenses or in front of the light source can prevent this effect.

Orwyn H. Ellis.

Bürki, E. The optics of contact lenses. Ophthalmologica 118:215-233, Oct.-Nov., 1949.

Most of the disadvantages of spectacle lenses are due to their finite thickness and their fixed position of about 12 mm. in front of a moving eye. The contact lens is free of most of these disadvantages and may be considered the most perfect visual aid. The paper deals specifically with the effect of contact lenses upon the size of the retinal images. In axial myopia the contact lens yields a larger retinal image than the spectacle lens. In curvature or refractive index ametropias the contact lens does not alter the size of the retinal images appreciably (as compared with the normal eve of the same axial length). In astigmatism the contact lens avoids the distortion of retinal images which is the typical result of spectacle lenses. From these mathematical findings the author draws theoretical conclusions concerning the correction of the various forms of anisometropia with contact lenses and the degrees of binocular sensory cooperation thereby attainable.

Peter C. Kronfeld.

Cohen, Henry. Subjective disorders of vision (excluding those due to local ocular disease), Tr. Ophth. Soc. U. Kingdom 68:3-12, 1948.

Subjective disorders of vision arise from disturbances of function due to deranged physico-chemical mechanisms or psychologic disturbances. The act of seeing involves two chains of events, the physicochemical and electrical changes which accompany the transmission of stimuli from the eye to the occipital cortext, about which much is known, and the process by which these cortical changes lead to the act of "seeing," of which we are profoundly ignorant.

Subjective disorders may have both physical and psychic causes and more than one site may be affected by the same pathologic agent. Arteriosclerosis, for example, may disturb retinal as well as cortical function. Subjective disorders can usually be made known only through speech; thus "blurred vision" may indicate either blurred outline or diplopia

or halo or even a visual hallucination. Evestrain is not an uncommon complaint in general fatigue from lack of rest, insomnia, malnutrition, toxemias and in psychogenic asthenias. The awareness and abnormal prolongation of afterimages may occur with fatigue. Blurred distant vision may be found in miosis due to morphine, eserine, tabes dorsalis or a general disease such as hypoglycemia; blurred near vision by mydriasis from belladonna poisoning, dehydration or lenticular opacities. Diplopia, shifting or distorted vision, chromatopsia, visual hallucinations, photophobia, muscae volitantes, and varying degrees of blindness all have subjective qualities, which may be due to some affection of the visual mechanisms or mimicked by psychogenic disturbances. Psychologic disturbances may also accompany organic disease, the final analysis of which will remain unexplained because our knowledge of fundamental problems of vision, especially in the psychological field, is limited.

Beulah Cushman.

Comberg, W. Can anisometropia be useful? Klin. Monatsbl. f. Augenh. 116: 18-22, 1950.

Anisometropia may be advantageous inasmuch as one may correct the one eye for distant the other eye for near vision in unilateral myopia, anisometropic hyperopia and bilateral aphakia, especially when the patient had been prevented from seeing binocularly for some time.

R. Grunfeld.

Druault, A. Phenomena of diffraction of the eye, an experimental comparative study. Arch. d'opht. 10:333-343, 1950.

The colored rings produced in the human eye in various normal and pathologic conditions result from different forms of diffraction, the optics of which are discussed in detail. The author reports on the experimental production of the rings by different diffraction screens. He states that the size of the rings, as seen by the eye, depends in part on the position of the diffracting element in the eye and that the size can be used to estimate the position of this element. The article is illustrated by two colored plates containing six figures. Phillips Thygeson.

Eckel, Kurt. The individual variations of scotopic visual acuity as determined with the nyctometer of Comberg. Ophthalmologica 119:364-373, June, 1950.

Comberg devised the nyctometer (Deutsche ophth. Gesellschaft 1940) for the purpose of determining visual acuity under scotopic conditions. Eckel studied the test-retest consistency of the data of the same experienced observer. The importance of calibration of the light source is stressed.

Peter C. Kronfeld.

Krahán, A. Adaptometry of isoptershaped retinal zones. Ophthalmologica 119:204-220, April, 1950.

The dark adaptation of bandshaped retinal zones, the course of which is parallel to typical isopters are quantitatively studied. Such zones contain retinal elements of similar sensitivity to light. During the exposure the "temptation" to change the direction of gaze is reduced to a minimum if a red central fixation point is offered. Such adaptometry is probably exact as far as constancy of the tested area is concerned. The author constructed a special apparatus for the study of a zone with an eccentricity of 45° on the nasal and of 60° on the temporal side. The same apparatus served for adaptometry of a circular zone of about 80 eccentricity and of the center itself. The apparatus could also be used for the study of dark adaptation of certain zones after or during the exposure of other zones of the retina to light. The studies revealed a number of interesting relationships between the peripheral and central retina which are in

close agreement with the findings of other authors.

Of clinical interest were the findings in amblyopia ex anopsia and in glaucoma. In the former the light threshold of the cones seemed to be increased to about the same extent as the visual acuity was reduced. In two cases of unilateral squint the light threshold of the rods was found to be lower in the amblyopic than in the normal-sighted eye. Some eyes with chronic glaucoma showed a peripheral adaptation curve of normal shape but in abnormally high position, which, according to Mandelbaum, indicates a disturbance of conduction rather than of photoreception, others had delayed peripheral Peter C. Kronfeld. adaptation.

Kraupa, Ernst. Double light sources for ophthalmoscopy and biomicroscopy. Ophthalmologica 118:318-320, Oct.-Nov., 1949.

Purkinje's entoptic phenomenon of the visibility of the retinal arterial tree has its ophthalmoscopic correlate in the form of actual vessel shadows which the author has observed in selected cases by means of a binocular ophthalmoscope of the Gullstrand type equipped with an arc light instead of the usual incandescent bulb. If the direction of the incident light is changed, the shadow wanders too. If two light sources are used, a double Purkinje phenomenon can be observed entopically. Double light sources may prove of practical diagnostic value in ophthalmoscopy as well as in biomicroscopy. Peter C. Kronfeld.

Lebensohn, J. E. A simplified astigmometer, Arch. Ophth. 43:905-907, May, 1950.

A description of this astigomometer and its use is given. Its applicability to the Crisp-Stine method is discussed.

Ralph W. Danielson.

Lo Cascio, G., and De Leonibus, F. The curvature of the posterior surface of the

cornea. Giorn. ital. oftal. 3:81-94, March-April, 1950.

Using Nordenson's technique as simplified by Berg, the authors have determined the curvature of the postcorneal surface in four astigmatic and four nonastigmatic eyes. Despite the number of observations made, it is clear that the deformation of the anterior corneal surface corresponds, almost constantly, to a similar astigmatic deformation of the posterior corneal surface, and that the astigmatism of the anterior corneal surface is in part neutralized by an analogous deformation of the posterior surface.

Vito La Rocca.

Mills, D. A. A system of remote control applied to astigmatic dials. Arch. Ophth. 43:912-913, May, 1950.

Subjective testing for astigmatism, accomplished by dials of the type made popular by Lancaster and Regan, is widely practiced. However, considerable effort is required in the selection of the proper axis on dial 1 and in the adjustment of dial 2 to that axis. A suitable method whereby these maneuvers may be accomplished by remote control is here described.

Ralph W. Danielson.

Nordlow, W. The accuracy of the objective and subjective method of determining the refraction of the eye. Acta ophth. 27:349-378, 1949.

The literature on the comparative evaluation of refractive data obtained sciascopically in cycloplegia and subjectively by Donder's method is reviewed, the conclusions critically analyzed and the sources of their inaccuracy demonstrated. The objective of this study was to determine statistically a reliable correlation between the data obtained by the two methods. The eyes of almost 200 patients were tested. The technique of the examinations, the theory of sciascopy and the sources of error in both methods are described in detail. The results of the

tests are analyzed statistically and the standard error for both methods calculated. As a practical deduction from these data the author states that in 77 percent of cases the reduction of the cycloplegic sciascopic finding by .66 diopters assures one that the hyperopia will not be overcorrected. If the sciascopic data exceed the subjective findings by more than .75 diopters one may suspect that all hyperopia has not become manifest. In 23 percent of cases, however, the sciascopic data may exceed the subjective findings by as much as 2 diopters, and vet the subjective test will represent the actual refraction of the eye. (1 figure, 2 graphs, 13 tables) Ray K. Daily.

Nugent, M. W. The Tuohy corneal lens. A second report. Arch. Ophth. 43: 232-237, Feb., 1950.

Approximately 600 patients have been fitted with the Tuohy corneal lens, and this paper represents a second report on the current experience. Apparently the new lens offers the advantages of greater comfort, reduced blurring and longer tolerance. The lens consists of a corneal portion only, and no accessory fluid is needed. Twenty cases of keratoconus have been fitted with this lens. The details of the fitting procedure are described.

John C. Long.

Rappaport, O. The principle and the phenomena of skiascopy. Ophthalmologica 118:234-253, Oct.-Nov., 1949.

The phenomena of retinoscopy are more easily understood if the light spot on the examinee's retina is considered as the light source with multiple, multicentered pencils of rays emerging from it. The name cinemascopy is proposed instead of the confusing and inappropriate term skiascopy. Peter C. Kronfeld.

Roessler, F., and Prskavec, F. The treatment of overactive accommodation.

Ophthalmologica 119:193-203, April, 1950.

Among the accommodative asthenopias there are, in principle, two possibilities: deficiency of accommodation due to a faulty impulse or an unyielding lens, and overaction of accommodation due to an impulse that is too strong for the visual task to be performed. The former condition yields easily to glasses, whereas the latter condition is often made more annoying by glasses. The primary site of the latter, "nervous" asthenopia, is unknown. After trying various drugs the authors discovered that dihydroergotamine taken orally had a beneficial effect upon overaction of accommodation. The drug used in this work was the dihydroergotamine solution of Sandoz of which the patients took 15 drops 2 or 3 times daily. Six case reports support the authors' contention of the effectiveness of sympatholytics in overaction of ac-Peter C. Kronfeld. commodation.

Santoni, A. The shape of the anterior surface of the cornea in high myopia. Giorn. ital. oftal. 3:3-16, Jan.-Feb., 1950.

In six highly myopic eyes, there was a central area of the cornea of which the main sections had a spherical curvature. This area was sometimes wider than in emmetropic eyes, and symmetrically disposed in the vertical and horizontal main sections. At the periphery of this area there was a normal tendency to flattening, but not with peculiarities of a physiological flattening.

Vito La Rocca.

Stanworth, A., and Naylor, E. J. Haidinger's brushes and the retinal receptors. Brit. J. Ophth. 34:282-291, May, 1950.

In 1844 Haidinger described an entopic phenomenon seen in polarized white light. Yellow and blue "brushes," the yellow ones parallel to the plane of polarization, are seen about the fixation point. Four theories of origin have been advanced.

They are ascribed to multiple refractions at the bounding surfaces of the transparent media, to the action of the media as doubly refracting plates, to the action of the radial fibers in the macular region as an analyser, and to subtotal reflection of rays that fall obliquely on the cones. All fail to explain the existence of the blue brushes as a positive phenomenon and in all the modern knowledge of the birefringence and dichroism of the retina is ignored. The authors suggest that the structures concerned in analysing the light are the blue receptors which could be dichroic owing to a regular arrangement of the molecules of the "blue substance" similar to that of the molecules of the visual purple in the dichroic rods. It is postulated that this dichroic pigment within the receptors is oriented radially in the macula and that the blue receptors, lying in the direction of the electric vector would absorb the incident blue light giving a sensation of blue. The light would be only weakly absorbed by the perpendicular blue receptors and therefore the preponderance of stimulation of the remaining retinal receptors would result in the complementary sensation of vellow. Morris Kaplan.

Stenstrom, Solve. A variable cylinder on Stokes' principle for the testing of astigmatism. Acta ophth. 27:379-384, 1949.

The author describes a contrivance to improve the efficiency of the cross cylinder. It consists of a plus 0.5 diopter and a minus 0.5 diopter lense mounted in a frame which fits the ordinary trial frame. The lenses are rotated by a spiral spring regulated by a piston built into the handle of the instrument. The strength of the cylinder can be varied between 1 and 0.5 diopter by a catch. It is claimed that rotation with this contrivance is smoother and quicker, and that it affords in addition a neutral lens without any cylindric

component for use in comparison. (1 figure) Ray K. Daily.

Stenstrom, Solve. The astigmatism of the refractive system of the eye and its components. Acta ophth. 27:455-474, 1949.

Early studies, which because of technical difficulties were not accurate, have shown that the lens usually has a slight astigmatism against the rule. The development of Rushton's method for measuring the optical axis provided a procedure, which when used in combination with other ophthalmometric methods permits accurate determination of the refractive power of the two principal meridians of the lens. The material for this investigation comprises 282 eyes of patients between 20 and 35 years of age. A detailed analysis of the tabulated and charted data shows the average lenticular astigmatism to be 0.64 against the rule. There is less variation in the lenticular than in the corneal astigmatism, and it is less influenced by such factors as the refraction of the eye and the total astigmatism. The stability of its refraction is attributed to its protected position in the interior of the eyeball, which shields it from exposure to external factors which might affect its form. There is a moderate negative correlation between the lenticular and corneal astigmatism, the former neutralizing the latter. The difference in the refraction of its two principal meridians is not identical with that of the total astigmatism. Even eyes without astigmatism show an average difference of 0.1 diopter, the result of which is a slightly greater magnification in the vertical than in the horizontal meridian. Ray K. Daily.

Trantas, A. Some entoptic phenomena. Ophthalmologica 118:305-317, Oct.-Nov., 1949.

The author describes the phenomenon of "auto-choroidopsie," that is of entoptic visualization of one's own choroid. The phenomenon is elicited by turning the eye down and placing the top of a transluminator against the upper lid in a position corresponding to a point on the sclera 12 to 14 mm, behind the limbus. Under these conditions one sees one's own choroid in the form of red bands separated by dark spaces. If the transluminator is placed against the sclera overlying the ora serrata the typical Purkinje phenomenon is seen. If two transluminators are applied over the ora serrata, one nasally and the other temporally, the author still sees only one arterial tree which does not seem to change position if one of the transluminators is turned off. These observations would tend to refute the convention explanation of the Purkinje phenomenon, namely that it is due to vessel shadows.

Upon first opening his eye at dawn the author perceives his blind spot as well as his physiological central scotoma entopically.

Peter C. Kronfeld.

Williams, Denis. Subjective disorders of vision, Tr. Ophth, Soc. U. Kingdom 68:13-26, 1948.

The author points to the result of studies in which a visual pattern is perceived as a whole, the figures related to each other against a background being so integrated that the complete picture is perceived. This integration leads to perfect depth perception with uniocular vision as the result of neural mechanisms in the higher visual association areas of the cerebral hemispheres. Therefore perception, as opposed to seeing, which depends only on the integrity of the lower visual structures from the eyes through the visual pathways to the visual cortex in the calcarine fissure, is studied in different ways. Study of the lower function involves exact measurement of visual acuity in the fields of vision, while that of the higher calls for verbal description and

analysis of the nature of the picture perceived.

The explanation for sparing of the macula in subjects with homonymous hemianopia has not been satisfactorily explained. Serious objections are made to the three main theories that have been advanced, that of 1, bilateral representation of macular fibers (Wilbrand) 2, of diffuse representation of macular fibers (Monakov) and 3. of failure of attention to the central object used for fixation. These theories take no cognizance of the great mass of nervous activity which translates the action potentials of crude sight into the pattern of intelligent perception. The author reports a patient whose attention to the blind half of his field with substitution of gazing for fixation resulted in macular sparing. A total lesion of one visual pathway can be compensated for by modifying the way the remaining pathway is used. (6 figures)

Beulah Cushman.

Zeeman, W. P. C. The horopter problem. Ophthalmologica 118:254-275, Oct.-Nov., 1949.

The variability of all experimentally determined horopters and their close dependency upon the specific circumstances of the experiment speak against a strict, point-to-point correspondence. Panum's concept of corresponding circles of sensation conforms better with the experimental findings. Corroborating evidence is quoted from the work of Roesch (Physiologie et géométric de la vision binoculaire et des mesures stéréoscopiques. Actualités scientifiques, Paris Zeeman then presents systematically and in considerable detail, the phylogenetic development of the organization of the visual pathway from completely separate to, at first, partly and then largely overlapping cortical retinal representations. These developments in the visual sphere correlated with the evolution of other

closely related sensory and motor functions, convey a better understanding of binocular sensory cooperation than the concept of a strict, innate, point-to-point correspondence. Peter C. Kronfeld.

## 5

## DIAGNOSIS AND THERAPY

Allen, J. H., and Allen, L. A buried muscle cone implant. 1. Development of a tunneled hemispherical type. Arch. Ophth. 43:879-890, May, 1950.

The development of a hemispherical buried muscle cone implant with tunnels for the individual rectus muscles is traced. and an implant and the surgical procedure are described. This implant is completely covered by conjunctiva and Tenon's capsule. Danger of extrusion is reduced. Infectious agents cannot pass readily into the cavity occupied by the implant. The tissues in the vicinity of the muscle cone are supported in a manner which assures a satisfactory cosmetic result. Although the extent of movement imparted to the prosthetic eye with this type of implant is not so great as with the partially covered implant and integrated prosthesis, short and immediate movement is approximately as good, and therefore adequate for practical purposes.

Ralph W. Danielson.

Amsler, M., and Huber, A. Darkfield and ultramicroscopic examinations of the freshly drawn aqueous. Ophthalmologica 118:450-460, Oct.-Nov., 1950.

The reader is first referred to the classical paper on the cytology of the ocular fluids (Graefe's Arch. 100:29, 1919) by A. Brueckner to whom volume 118 of Ophthalmologica, including the paper under review, is dedicated in celebration of his 70th birthday. Brueckner's studies have been continued and extended by Amsler and Verrey who investigated systematically the morphology of the cells found in the freshly drawn aqueous of

man (Verrey, F: A study of the morphological elements in the diseased aqueous, Librarie medicale, Lausanne, 1945). The paper under review represents a further extension of these cytological studies. The freshly drawn aqueous of human eyes with various forms of iridocyclitis is placed on a slide and without any fixation or staining examined with the ultramicroscope. Some of the authors' findings are recorded in very impressive photomicrographs showing endothelial and exudative cells in various states of cellular activity. Peter C, Kronfeld.

Anderson, J. Ringland. Aids to corneal staining. Ophthalmologica 118:444-449, Oct.-Nov., 1949.

The history of the method of corneal staining for diagnostic purposes is reviewed. The method can be refined by using light from the violet end of the spectrum as the exciting light and a yellow filter for making the actual observations.

Peter C. Kronfeld.

Blatt, N., and Athanasiu, M. A typical deformation of the optic canal in an osteoma of the sphenoid. Ophthalmologica 119:137-145, March, 1950.

In a 55-year-old white woman "a systemic disease of the bone" (of unspecified nature) produced a large bony, radiologically osteoma-like tumor of the left sphenoid with unilateral optic atrophy and exophthalmos. The roentgenologic examination of the optic foramen revealed a very unusual deformation: an almost square lumen with crenated edges. The course of the disease is not stated. The actual nature of the tumor was, apparently, not determined by either surgical exploration or autopsy. The author stresses the diagnostic value of exact roentgenographic visualization of the Peter C. Kronfeld. optic foramen.

Chace, R. R., and Lafayette, J. H. A modified film carrier for the Zeiss-

Nordenson fundus camera. Arch. Ophth. 43:910-911, May, 1950.

The advantages of a new modified film carrier are discussed and shown in diagrams. Ralph W. Danielson.

Costenbader, F. D. The accommodometer, Tr. Am. Acad. Ophth. pp. 362-364, March-April, 1950.

An instrument designed to aid in determinations of punctum proximum, near visual acuity, and as a near fixation object in the study of strabismus is presented. The instrument consists of a white rotary disc on which are printed graded sizes of "illiterate E," silhouettes, letters and words corresponding to different degrees of visual acuity as determined at 1/3 meter. The disc is shielded in a black plastic casing, having a circular window facing the examinee through which only one figure at a time is seen, and a horizontally oval window on the opposite side through which the examiner sees the figure seen by the examinee, and the next larger and smaller one. The instrument can be held and the disc rotated with one hand.

Chas. A. Bahn.

Craig, P. C. Suspension of upper lid during intraocular operations. Arch. Ophth. 42:461-462, Oct., 1949.

A long silk suture is inserted into the skin of the upper lid just above the ciliary margin in such a way that four points of traction are obtained. The needle is introduced 8 mm. to one side of the center of the lid and carried under the skin for 5 mm. where it is brought out. It is now re-introduced 6 mm. from the point of exit and emerges 5 mm. from the point of entrance. A loop is formed of the exposed suture. The two ends of the suture and the loop are held by an assistant during intraocular surgery, making the use of a speculum unnecessary. John C. Long.

Davson, H., and Purvis, C. A simple manometer for the continuous measurement of intra-ocular pressure. Brit. J. Ophth. 34:351-354, June, 1950.

Apparatus for the continuous measurement of intraocular pressure is described in detail. The fluid loss in the system is minimal and the manometer is sufficiently sensitive to show the normal pulsation which corresponds to the arterial systole. The instrument consists of a manometer which moves a roller upon which are mounted two mirrors. A beam of light reflected from the mirrors gives two spots on a suitably placed scale.

Orwyn H. Ellis.

Dejean, C. Description of three new instruments. Arch. d'opht. 10:65-67, 1950.

Dejean reports three new surgical instruments. The first, a special forceps, is designed to remove exudate from the cilia by a comb-like action. Each arm of the forceps has eight teeth which are kept from coming completely into apposition by a metal stop, thus allowing the cilia to slide in between. The second instrument is a curved loop resembling that of Snellen but smaller, more curved, and narrower. The third instrument is an iris spatula with two small, pointed projections near its end. By a rotating movement the projections can engage the iris stroma and return the iris to proper position after round pupil extraction. Since the projections are not curved they easily disengage, allowing the spatula to be removed without difficulty.

Phillips Thygeson.

Doggart, James. Subjective disorders of vision, Tr. Ophth. Soc. U. Kingdom 68:27-33, 1948.

The author discusses such visual disturbances as diplopia, field defects, defective vision, defective night vision, photophobia, and colored vision in patients without ocular lesions but aware of symptoms. Partial or complete diplopia may be the result of an orbital lesion.

When the onset is rapid the cause is frequently an intracranial injury or a disease such as disseminated sclerosis, tabes, diabetes, ophthalmic zoster or myasthenia gravis. The field can contract without attracting the patient's notice even when the defect nearly encroaches upon the fixation point. Sudden obliteration is not likely to pass unnoticed. Disturbance of orientation is often the result of injury when the parieto-occipital region of the cortex is damaged. This loss of orientation from severance of links between visual perception with other afferent impressions can be unilateral. Brain stem lesions of the vestibular apparatus and of the oculomotor nuclei region are apt to produce headaches, giddiness and blurred vision when reading or looking at moving pictures. Beulah Cushman.

Donaldson, D. D., and Cogan, D. G. A fixation aid for slit lamp biomicroscopy. Arch. Ophth. 43:555-556, March, 1950.

To permit a ready variation in fixation, the authors have found the following procedure satisfactory for all but one-eyed patients. Two mirrors about 5 cm. in diameter are attached to the chin rest base by means of a flexible cable in such a way that each mirror may be placed in front of one eye in any position.

R. W. Danielson.

Feinberg, S. M. Drugs in allergy. Tr. Am. Acad. Ophth. pp. 283-286, March-April, 1950.

Vasoconstrictors, local anesthetics, sedatives and antihistaminic drugs employed in the management of ocular allergies should be used with the understanding that they are only supportive and palliative devices. The mainstay of successful treatment consists of identification and elimination of the causative antigen. In chronic allergic states, prolonged use of vasoconstrictors such as privine, ephredrine, and neosynephrine

is followed by secondary dilatation and more edema and a vicious circle is established. Sedatives and local anesthetics should be used sparingly, if at all. The antihistaminics are valuable in alleviating symptoms and in partially controlling the antigen-antibody reaction. Side reactions such as drowsiness, vertigo, headache and gastrointestinal disturbances are encountered, and fatalities may result from indiscriminate use of the drugs.

Gustav C. Bahn.

Girard, L. J. The Lancaster-Regan astigmatic dials with illumination and remote control. Tr. Am. Acad. Ophth. pp. 364-366, March-April, 1950.

The Lancaster and Regan astigmatic dial charts are operated by two synchronized motors; the dials are attached to one motor placed at the far end of the refraction lane, the control motor and light switches at the examiner's end of the lane. The dials are housed in a metal cabinet and are illuminated by two 14-inch circular neon tubes. The instrument facilitates subjective determination of astigmatic errors because it eliminates the necessity of crossing the room in order to adjust the dials.

Gustav C. Bahn.

Goff, J. L. Transformer for the A O "giantscope." Arch. Ophth. 43:553, March, 1950.

In order to facilitate the portability of the A O "giantscope," a transformer small enough to be installed in the original box is described. R. W. Danielson.

Gordon, D. M., and McLean, J. M. Effects of pituitary adrenocorticotropic hormone (ACTH) therapy in ophthalmologic conditions. J.A.M.A. 142:1271-1276, April 22, 1950.

Because of its therapeutic value in acute inflammatory conditions of structures composed of collagenous and mesenchymal tissues, adrenocorticotropic hormone was given with dramatic response to patients with iridocyclitis and choroiditis. Temporary benefit was obtained in a case of retinitis pigmentosa. After the administration of the hormone all six patients showed a definite reduction in the number of circulating eosinophils. A temporary hypertension was noted in two patients, one of whom also had a glycosuria; another had temporary abdominal distension. A case of corneal dystrophy and another of secondary glaucoma failed to exhibit any favorable response to a short course of treatment. (7 figures)

Herman C. Weinberg.

Harms, H. Future developments in perimetry. Arch. f. Ophth. 150:28-57, 1950.

This study especially considers size and brightness of the test object and the state of adaptation of the examined person. Reference is made to the work of Traquair, Ferree and Rand, and Sloan and Blair.

Ernst Schmerl.

Harrington, D. O. Harrington pocket chart. Tr. Am. Acad. Ophth. p. 376, March-April, 1950.

A six inch plastic rule with a reduced Snellen chart printed on one surface and pictures of graded sizes printed on the other is presented. A red glass or Maddox rod is mounted in a hole cut in one end of the rule, and a 14-diopter lens in the other.

Gustav C. Bahn.

Hauck, D. L. A soundproof case for the Castroviejo suction kit. Arch. Ophth. 43: 908-909, May, 1950.

Many surgeons have found the Castroviejo erisephake a fine instrument for cataract extraction, but owing to its excessive noise, it has been avoided by many operators. An encasing silencing box is described. The box absorbs all but a small amount of the noise; enough remains that the operator can comfortably tell when the pump is working.

Ralph W. Danielson.

Hobbs, H. E. The use of the ophthalmoscope. Clin. J. 79:124-128, May, 1950.

The advantages of direct and indirect ophthalmoscopy and a systematic method of examination are described.

Irwin E. Gaynon.

Hudson, J. R. The all-tantalum Cutler universal integrated implant. A modified technique for its introduction: case reports. Brit. J. Ophth. 34:251-258, April, 1950.

A modified technique for the introduction of the tantalum Cutler universal integrated implant is presented. In this procedure, after securing the isolated recti muscles to the implant, the tendon is split a few millimeters up to the silk suture which secures the tendon to the implant. This allows the slips of tendon to be attached and sewn together to form a ring at the edge of the implant. The conjunctiva is sewn over this. This forms a complete muscular ring and although probably converted to fibrous tissue at a later stage fulfills its function of firm attachment to the implant. There are no stitches to be removed after the operation and the socket is packed for seven days to prevent chemosis, and to aid in the attachment of the muscles to the tantalum mesh. The possibility of late extrusion is thereby lessened.

Orwyn H. Ellis.

Hymes, C. A new forceps and technic for the corneal transplant operation, Tr. Am. Acad. Ophth. pp. 357-360. March-April, 1950.

The author presents a forceps which clamps the cornea, lifting it away from the iris and lens, and which serves as a guide for the trephine blade during keratoplasty. The lower cup-shaped blade

is inserted into the anterior chamber through a limbal incision and the upper ring-shaped blade fits over the cornea. The shaft of the forceps is angulated so that the brow will not interfere with manipulation of the instrument. In the center of the cup-shaped blade is a 1.5mmhigh guide post which reinforces the corneal button and insures clean excision. A modification of the Green trephine is used with the forceps. Gustav C. Bahn.

Junès, Emile. Hemeralopia of hepatic origin, healed by intravenous injections of pure codliver oil. Arch. d'opht. 10:58-61, 1950.

A 40-year-old man, with hepatic insufficiency, normal central vision, and progressively increasing night blindness, was treated with 15 intravenous injections of codliver oil, spaced at five-day intervals. The initial dose was 0.5 cc. This was increased by 0.25 cc. each time until a maximum of 2.0 cc. was reached. After the fifteenth injection the patient stated that he was completely free from symptoms; no follow-up examinations were made. The author states that he has used this treatment with success in severe corneal ulceration, phlyctenular keratitis, tuberculous keratitis, and retrobulbar neuritis. The possible mechanisms of action are discussed.

Phillips Thygeson.

Kettesy, A. Modification of Imre's step. Ophthalmologica 119:146-148, March, 1950.

Triangular defects of the skin of the lower lid can be repaired after the method of Burow-Elschnig by sliding into the lid a flap from the region temporal to the outer canthus. The method works well except for a slight to moderate sagging of the new, reconstructed (temporal) portion of the lid border. To correct this deformity Imre devised his "step": the flap-forming incision starts out as an

intermarginal one in the lid and, just outside the outer canthus, makes a step upward, about 2 mm. in height and 6 mm. in length. Then the incision returns to the level of the usual, slightly upward temporal incision of Burow-Elschnig. Kettesy has modified the Imre incision, in that he makes the step higher and maintains this higher level to the very end of the again upward-curved incision. One excellent operative result is illustrated.

Peter C. Kronfeld.

Klein, M. Appliances. A new model of streak retinoscope. Brit. J. Ophth. 34:391, June, 1950.

A new retinoscope is presented. The disc for rotation of the streak and the cuff for focusing the beam can be manipulated with one hand. An anti-glare hood permits retinoscopy in daylight. A scale on the top of the handle indicates the position of the streak.

Orwyn H. Ellis.

Kornerup, T. Damage to the visual organs resulting from typhoid inoculations. Acta ophth. 27:383-391, 1949.

The reported neurologic complications of typhoid inoculations are reviewed. Ten cases of ocular damage in a group of 50 cases of neurological damage reported by Bjerner in 1945 are reported briefly. Of the 10 patients with ophthalmic complications 4 had optic neuritis, 1 optic atrophy, 3 temporary color blindness and 2 paresis of the extraocular muscles. The pathogenesis of these complications is as yet not understood, and the prognosis is usually good. Persons with a history of renal disorders, or with luetic or other chronic inflammatory diseases of the eyes should not be given typhoid inoculations.

Ray K. Daily.

Kozlowski, Bogumil. The method of localization of tears in retinal detachment. Klinika Oczna 18:375-388, 1948.

The author presents his own method for the exact determination of the tear, the visual angle and the visual axis, the position of the tear and its distance from the ora serrata and the limbus. Exact instructions are given as to the methods of determining all these findings.

Sylvan Brandon.

Krakau, C. E. T. A simple apparatus for measuring level differences in the eyeground. Acta ophth. 27:263-265, 1949.

The device which is described for use with the simplified Gullstrand ophthalmoscope affords a determination of level differences in the eyeground as low as 1/5 diopter. (1 figure) Ray K. Daily.

Kraupa, Ernst. Reading aids for the visually defective and the blind. Ophthal-mologica 118:945-948, Oct.-Nov., 1949.

Ordinary print can be magnified 30 times and thereby made legible for patients with very low visual acuity by projecting the print on a screen and viewing the projected image through telescopic spectacles. The Morse code has the great advantage over Braille that most people know it and therefore would not have to learn anything new in case of blindness acquired late in life. A simple buzzer device could serve to convert a Morse text into sound.

Peter C. Kronfeld.

Krimsky, Emanuel. A multiple prism holder. Tr. Am. Acad. Ophth. p. 370, March-April, 1950.

The author presents a metallic rack into which can be clamped one or two standard size glass or plastic prisms.

Gustav C. Bahn.

Krimsky, Emanuel. The stepladder prism. Tr. Am. Acad. Ophth. p. 369, March-April, 1950.

The instrument consists of a standard 40-degree plastic prism which has been cut in such a way that three prisms are formed with their apices falling along one edge of the square. The prismatic strengths of the steps are 10, 20 and 40 diopters.

Gustav C. Bahn.

Krimsky, Emanuel. Monocular eyeglass loupe with focal illumination. Tr. Am. Acad. Ophth. p. 371, March-April, 1950.

This clip-on type of monocular loupe consists of a 14 Diopter lens and a flashlight socket and bulb mounted on a heavy wire spring clamp. A connecting cord runs from the lamp to a battery handle which is carried in the examiner's pocket.

Gustav C. Bahn.

Lancaster, W. B. The red-green test. Tr. Am. Acad. Ophth. pp. 367-368, March-April, 1950.

The author presents a red-green test unit which consists of 1. a roller screen marked off into 70-mm. squares which subtend an angle of 2° at a working distance of 2 meters; 2. goggles which have a red plastic lens on the right side and a green lens on the left eye, and 3. two hand projectors, one of which projects a red bar, the other, green. The projectors are operated on 110 volts.

Gustav C. Bahn.

Lindberg, V. L. A calibrated light separator. Tr. Am. Acad. Ophth. p. 361, March-April, 1950.

An instrument designed for gross determination of macular function by two-point discrimination is described. Two equally illuminated ophthalmoscope bulbs are mounted on a metric scale. The lights may be separated from 0 to 10 cm. Macular function is graded as good, very good, and excellent if the patient can discriminate two lights 2 cm., 1 cm. and 0.5 cm. apart respectively, at a distance of one meter from the instrument.

Chas. A. Bahn.

Mata Lopez, P. The status of therapy of ocular tuberculosis. Arch. Soc. oftal. hispano-am. 10:265-294, March, 1950.

The literature is reviewed.

Ray K. Daily.

Meadows, S. P. The eye in relation to general medicine and neurology. Clin. J. 79:113-124, May, 1950.

Differential diagnosis of papilledema, optic neuritis, optic atrophy and retrobulbar neuritis is described. Supra- and infranuclear palsies, miasthenia gravis, and the common visual field defects are explained.

Irwin E. Gaynon.

Olson, J. A., Steffensen, E. H., Margulis, R. R., Smith, R. W., and Whitney, E. L. Effect of ACTH on certain inflammatory diseases of the eye. J.A.M.A. 142: 1276-1278, April 22, 1950.

Adrenocorticotropic hormone was administered in four cases of acute plastic iritis, in two of keratitis with anterior uveal tract involvement and in one case of recent chorioretinitis with absolute scotoma. The dosage varied from 185 to 432 mg. given over a period of 3 to 13 days intramuscularly in 10 or 20 mg. injections at intervals of 4 to 6 hours. All patients responded abruptly and favorably to therapy. Symptomatic relief and objective improvement was seen as early as the second hour after administration of the hormone. Glycosuria appeared in two patients and auricular fibrillation in one during treatment.

Herman C. Weinberg.

Osterlind, Gote. Ocular responses in protein shock therapy. Acta ophth. 27: 311-336, 1949.

A blunt trauma applied to the eye of a normal rabbit by the impact of a small steel ball falling from a height of 120 cm. produces prompt dilatation of the minute vessels in the traumatized sector of the iris, followed by a more widespread

dilatation in the whole iris and a rise in ocular tension. An increased permeability of the capillaries is demonstrated by a preliminary injection of trypan blue. The extent of the reaction can be markedly reduced by an intramuscular injection of boiled milk 42 to 72 hours before the trauma. In rabbits a milk injection also inhibits the normal reaction to histamine introduced through the skin. In order to determine the histamine reaction of the human skin before and after protein shock, 23 patients with acute or subacute iritis were tested with solutions of histamine before and after milk injections. The experiments demonstrated the ability of general protein shock to decrease the responsiveness of the cutaneous vessels to histamine, but its effect was more variable and irregular than in rabbits. The same inhibition was achieved by the intravenous injections of blood plasma from rabbits treated with milk injections. It is suggested that this inhibitory effect is probably due to some factor capable of inactivating histamine. It is present in blood plasma; it dialyses readily and is destroyed by boiling. Ray K. Daily.

Posner, Adolph. Illuminator and head rest for the tangent screen. Tr. Am. Acad. Ophth. p. 377, March-April, 1950.

The instrument consists of a 12-inch, 32-watt circline fluorescent tube mounted within a reflector and black housing. At the back of the housing is mounted a chin rest which can be moved from side to side, so that the eye being examined is placed in the center of the ring. The illuminator provides approximately 7 foot candles of fairly evenly distributed light on the screen.

Gustav C. Bahn.

Rochels, K. H. An instrument for objective determination of visual acuity. Klin. Monatsbl. f. Augenh. 116:31-34, 1950.

A black and white checker-board design in three sizes is printed on a paper

band which runs over two drums behind a screen. Three windows are cut in the screen, one for each design. Only one window is open at one time. The patient sees the rotating band through a tube and the examiner observes the nystagmus that results with a magnifying loupe. The drum is illuminated from behind. Only normal persons were examined thus far. For each design the speed of rotation and the distance from which the pattern is viewed when nystagmus is induced are correlated with the visual acuity. The author thus has empirically found a set of values for every visual acuity. The visual acuity of a simulant can be objectively ascertained by this means especially if the person is not aware that he is being tested for visual acuity.

R. Grunfeld.

Rogers, B. O. The problem of skin homografts. Plast. and Reconstr. Surg. 5: 269-282, April, 1950.

A homograft is one in which tissue is transplanted from one individual to another of the same species. Before 1910 a few successful homografts of skin had been reported but almost none since. Homografts are now used only as emergency dressings for the extensively burned patient. The graft takes well initially and seems to be accepted by the host for ten days to ten weeks or more but then loses its power to spread by epithelial proliferation from its edges and finally melts away. Although the homograft is lost, it serves as more than just a dressing to the burned patient; the patient is given a respite from the frequent painful change of dressings and he is restored to a more normal fluid balance. A solution of the problem of homografting would make possible the development of skin banks wherein grafts taken routinely from cadavers are ready for immediate application as emergency dressing.

Of the numerous hypotheses which have been advanced to explain the cause for the sloughing and the means by which permanently successful homografts may be obtained, three are outstanding.

1. The hemotologic hypothesis is based upon the supposition that the homografting of skin would be permanently successful if the principles underlying the homografting (transfusing) of blood were applied. The early investigative work to support this theory was performed during the time that only four blood group factors were known, but most recent work, both clinical and experimental, refutes this hypothesis.

2. The genetics-cellular hypothesis is based upon the idea that the response of the body of the host to the graft is a local tissue reaction founded upon genetic differences between the cells of host and donor. Most workers have reported lack of success when there was no genetic of familial relationship, but neglected to mention that they were unable to achieve success when a genetic similarity was present. The grafting between monozygotic twins is not true homografting but autografting.

3. The acquired immunity hypothesis has the largest amount of clinical and experimental work to prove or disprove it. Its supporters believe that the graft elaborates antigens and the resultant antigen-antibody reaction destroys the graft. The increased number of lymphocytes and plasma cells, the carriers and manufacturers of antibodies, favors the hypothesis in that the lymphocyte and plasma cells are only present near the time of sloughing.

Clinical evidence on the whole seems to contradict Medawar's experimental evidence on the acquired immunity hypothesis. The evidence for and against this hypothesis is circumstantial only.

A comparison of avascular epidermis grafts and corneal grafting raises many interesting questions that are impossible of answer at present.

Alston Callahan.

Rolf, D. E. Muscle hook. Arch. Ophth. 43:554, March, 1950.

This muscle hook has the following features: 1, a thin, narrow blade for ease in manipulation, 2, millimeter markings for quick estimation of the width and thickness of the muscle and rapid appraisal of the various measurements which are used in ocular surgery, 3, a scleral marker at the tip which eliminates the need for an extra instrument and 4, a blade which is long enough to allow the tendon of the muscle to be gently stretched over the surface for ease in suturing.

R. W. Danielson.

Ruedemann, A. D. Beta radiation in industrial ophthalmology, Tr. Am. Acad. Ophth. pp. 391-392, March-April, 1950.

Industrially acquired lesions of the cornea with glaucoma and vascularization have in many cases been successfully treated with radon, radium D. or one of the newer radioactive isotopes. Relief from photophobia and lacrimation, as well as cosmetic improvement and diminution in the density of leucomata were often obtained.

Gustav C. Bahn.

Saltzman, S., and Haig, C. Treatment of retinitis pigmentosa with cod liver oil injections and placental implantation. Arch. Ophth. 43:419-430, March, 1950.

This study did not confirm the reports of Filatov, for 47 patients with retinitis pigmentosa and 2 with retinitis punctate albescens were treated without significant improvement in visual acuity, visual fields, or light sensitivity.

E. J. Swets.

Schober, Herbert. A projector of testletters for subjective determination of exact and reproducible visual acuity. Klin. Monatsbl. f. Augenh. 116:22-31, 1950.

The author describes a projectograph of his own design. R. Grunfeld.

Scott, G. I. Some observations on clinical perimetry. Tr. Ophth. Soc. U. Kingdom 68:225-240, 1948.

The author gives his impressions of the value and use of perimetry in ordinary clinical practice. Clinical accuracy is essential and the results must be correlated with other data.

Beulah Cushman.

Segal, Pavel. Tissue therapy of Filatov observed at the eye clinic of the Warsaw University. Klinika Oczna 18:531-548, 1948.

The author discusses the history and the principles of Filatov's treatment with implantations of tissues. Numerous tissues and methods of preparation and implantation are described. According to Filatov any living tissue, animal or plant, when kept in adverse conditions produces some substances which stimulate recovery or improvement when implanted into a patient. In 95 patients 140 implantations of preserved amniotic membrane under the skin or conjunctiva were made in two years. Improvement was noted in one third of the patients, and failure in one half. Sylvan Brandon,

Spero, G. D. A new shoestring corneoscleral suture. Arch. Ophth. 42:463-464, Oct., 1949.

A corneoscleral suture with modified conjunctival flaps is described. A limbal incision is made between 11 and 1 o'clock and two conjunctival flaps are formed, one from 11 to 9 and the other from 1 to 3. A single 6-0 silk suture is knotted double. The needle is first introduced into the conjunctiva about 5 mm. above the limbus at 12 o'clock. A vertical bite is then taken in the episclera 2 mm. from the limbus. The needle is then reintro-

duced through the conjunctiva 2 mm. above the free border and brought out. A second suture, similarly knotted, is introduced vertically in the cornea 2 mm. below the limbus at 12 o'clock and brought out as close to the limbus as possible. After the lens is extracted, the central sutures are tied with a double loop.

John C. Long.

Spero, G. D. Lid expression forceps. Arch. Ophth. 43:914, May, 1950.

Expression of the lids is a valuable procedure in the treatment of blepharitis or blepharoconjunctivitis. If expression reveals considerable secretion, it should be done once or twice weekly for a number of weeks, until the secretion becomes minimal. A new forceps for this procedure is described.

Ralph W. Danielson.

Strampelli, B. Retrobulbar cocain injection to produce hypotony. Atti d. 37 Congresso Soc. oftal. ital. 10:336-339, 1948.

In order to produce effective and long lasting hypotony before an operation the author adds 0.5 cc, of a 5-percent cocain solution to the retrobulbar injection of 2.5 cc, of 3-percent procain with adrenaline. This type of retrobulbar injection together with the usual topical anesthesia causes a consistent hypotony.

Frederick C. Blodi.

Sysi, R. A simple device supplementary to the slit lamp to photograph the parts of the eye. Acta ophth. 27:403-408, 1949.

Sysi describes a device which permits the connection of a camera to one of the oculars of the slitlamp microscope for photography of the anterior ocular segment. (2 figures)

Ray K. Daily.

Sysi, R. A new method of closing the lacrimal canals. Acta ophth. 27:409-411, 1949.

Attention is called to the frequent fail-

ure of closing the canaliculus by cauterization because the epithelium has a tendency to reform and open the canal. The author was successful in two cases in which he excised a portion of the canaliculi through a skin incision and in addition cauterized the lacrimal puncta.

Ray K. Daily.

Theodore, F. H. Use of sodium propionate in the external infections of the eyes, J.A.M.A. 143:226-228, May 20, 1950.

Sodium propionate is stable, practically nontoxic, nonallergic and is effective against all the common bacteria and fungi affecting the external tissues of the eye. Irwin E. Gaynon.

Thorpe, H. E. Special forceps for use in corneal and scleral surgery. Tr. Am. Acad. Ophth. p. 374, March-April, 1950.

A forceps with fine shark-tooth serrations on the edge of one blade is presented. The tips of the forceps come to a point and the serrated teeth close on the opposing blade back of the tip, so that the cornea or sclera may be grasped with the side of the forceps. Gustav C. Bahn.

Thorpe, H. E. Streamlined slitlamp microscope objective. Tr. Am. Acad. Ophth. p. 375, March-April, 1950.

A short-nosed, streamlined binocular objective for use on any slitlamp in common use is presented. The shortness of the objective facilitates obtaining a more acute angle between the illuminating and observation systems in deep vitreous visualization and in gonioscopy.

Gustav C. Bahn.

Wagner, H. N., Jr. Objective testing of vision with use of the galvanic skin response. Arch. Ophth. 43:529-536, March, 1950.

A technique is presented for the objective testing of vision in man, monkey, cat and rat, with use of the conditioned galvanic skin response, and, in the case of animals, the catalepsy-producing drug bulbocapnine. R. W. Danielson.

Weinstein, P., and Forgács, J. Rutin and dicumarol in ophthalmology. Ophthalmologica 119:122-125, Feb., 1950.

In patients with obstruction of the central retinal vein rutin and dicumarol were used together, to reduce the prothrombin content of the plasma from one half to one third of normal. Rutin alone was used in cases of hypertensive retinitis, diabetic retinitis, Eales' disease and vitreous hemorrhages of undetermined cause. The results were very satisfactory, especially in cases of obstruction of the central vein and in Eales' disease. The results are not reported in detail, except for one case of venous branch obstruction in which vision improved from 5/50 to 5/6 within 5 weeks of combined rutin and dicumarol treatment.

Peter C. Kronfeld.

Weinstein, P., and Forgács, J. Experiences with Filatov's tissue therapy. Ophthalmologica 119:154-156, March, 1950.

The basic concept underlying Filatov's tissue therapy is that normal tissue, if stored at low temperatures, produces substances which protect the normal tissue against necrosis and, at the same time, are capable of stimulating tissue functions under conditions other than exposure to cold. These substances are called biogenic stimulators. The standard method of producing them is to store a fresh human placenta at 4°C. for five days and then to autoclave it at 120°C, for one hour. The material is used therapeutically by implanting small pieces of it subconjunctivally.

The treatment was used in 11 cases of chronic inflammation of the anterior segment (keratitis and iridocyclitis) and in 19 cases of partly degenerative, partly vascular fundus alterations. The results were not given in detail, but the authors seem to be favorably impressed with the effect of such treatment upon torpid keratitides. From the observations reported by the authors no definite conclusions can be drawn.

Peter C. Kronfeld

Woods, A. C., Wood, R. M., and Naquin, H. A. Studies in experimental ocular tuberculosis. XIII. Effect of streptomycin and promizole in experimental ocular tuberculosis in the normal rabbit. Arch. Ophth. 43:834-844, May, 1950.

The effect of streptomycin and promizole on experimental ocular tuberculosis in 15 normal rabbits is reported. Previous studies of the effect of these therapeutic agents on immune-allergic animals has been reported, and the present report presents a much more severe test of the therapeutic efficacy of these agents. A presumptive complete cure of 40 percent of the animals was achieved. The action of streptomycin and promizole on ocular tuberculosis is bacteriostatic and bacteriocidal, and operates independently of the immunity factor. There was complete control of visible inflammatory activity in all 15 animals during the period of treatment. E. J. Swets.

Woods, A. C., Wood, R. M., and Naquin, H. A. Studies in experimental ocular tuberculosis. XIV. Failure of aureomycin to affect the course of ocular tuberculosis. Arch. Ophth. 43:845-848, May, 1950.

In view of somewhat conflicting evidence, it seemed pertinent to evaluate the effect of aureomycin on the progress of experimental ocular tuberculosis in the rabbit. In these experiments, aureomycin had no deterrent effect on the development or course of ocular tuberculosis in the normal rabbit.

E. J. Swets.

## OCULAR MOTILITY

Bietti, G. B. Transplantation of the levator palpebrae in paralyses of elevation. Ophthalmologica 119:56-62, Jan., 1950.

To the well-established techniques of transplantation of extraocular muscles Bietti adds a new procedure which, in principle, makes the levator palpebae work as an elevator of the globe. Through a T-shaped conjunctival incision the insertion of the levator at the upper border of the tarsus is exposed, two paracentral vertical strips of levator are dissected free and their distal ends connected with the superior rectus. The author used this method successfully in one case of congenital and familial total ophthalmoplegia.

Peter C. Kronfeld.

Casari, Gianfranco. Retinal correspondence and orthoptic therapy in concommitant strabismus. Rassegna ital. d'ottal. 19:101-139, March-April, 1950.

The author reports upon his examination of the relation of retinal correspondence in 90 individuals with concommitant strabismus who were treated by orthoptic exercises, with and without surgical intervention. He concludes that retinal correspondence is necessary before commencing orthoptic treatment. After developing correspondence, exercises and surgery are indicated. The 90 cases are presented in some detail and the results analysed.

Eugene M. Blake.

Chamlin, M., and Billet, E. Ophthalmoplegia and pigmentary degeneration of the retina. Arch. Ophth. 43:217-223, Feb., 1950.

Three cases of chronic, progressive external ophthalmoplegia with associated atypical pigmentary degeneration of the retina are presented. Seven similar cases are found in the literature. In all cases of external ophthalmoplegia, especially those in which tests for myasthenia with neostigmine or physical signs of intracranial tumor or aneurysm are lacking, a careful search should be made for early pigmentary degeneration of the retina, which will help identify a degenerative disease. John C. Long.

Dimsdale, Helen. Ocular palsies due to infection of the nasal sinuses. Tr. Ophth. Soc. U. Kingdom 68:197-201, 1948.

The author presents patients who showed involvement of ocular muscles associated with acute frontal sinus infection and acute suppurative sinusitis of the sphenoidal sinus. The anatomic relation of the third, fourth and sixth nerves to the sinuses is reviewed. Palsies may result from an edema with secondary proliferative changes in the region of the superior orbital fissure which are an extension of pachymeningitis. Rapid improvement follows early treatment of the affected sinuses.

Beulah Cushman.

Fischer, Hermann. Physiologic limits of the horizontal movements of the eyes. Arch. f. Ophth. 150:144-156, 1950.

254 patients were stidied with the help of the perimeter. The mean value for abduction was found to be 45°, for adduction 52°. The ocular motility diminishes as much as 14° with increasing age and was also found slightly less in myopes than in emmetropes and hyperopes.

Ernst Schmerl.

Girling, W. N. M. Eye headache and discomfort not corrected by glasses. Northwest Med. 49:110-111, Feb., 1950.

The author emphasizes the need for careful muscle-balance tests and the use of orthoptics in eye headaches not corrected by glasses. Donald T. Hughson.

Hugger, Hubert. Vomiting after strabismus operation. Klin. Monatsbl. f. Augenh. 116:81-83, 1950. Vomiting is common after strabismus surgery. It lasts 24 hours or longer. It follows only muscle strengthening and never muscle weakening operations. It is not a vagus pressure symptom for the vagus is nowhere pressed upon. It has a direct relation to the size of the angle of strabismus and occurs only if the angle of deviation is greater than 20 degrees.

On the surface of muscle-fibers there are sensory nerve endings which surround the muscle in the form of spindles. The nerves follow the oculomotor nerve and are connected with the mesencephalic tract of the trigeminus which lies in the vicinity of the vagus nucleus. The oculomotor and trigeminal nerves have other connections in the sinus cavernosus. After an advancement operation the muscle fibers are under a stronger passive tension. As the anesthesia wears off the over-flow of the strong stimulus to the vagus nucleus induces the vomiting reflex.

R. Grunfeld.

Isola, Washington. Visual function and postural function. Ann. d'ocul. 183:408-419, May, 1950.

"The internal rectus is without doubt an extensor muscle." This and several other interesting concepts in this contribution should be critically reviewed because of their basic importance. The external rectus is considered as a flexor and the dominant muscle in all lateral movements. An interesting experiment is presented to illustrate ocular dominance. If a red glass is placed before the left eve which has a paralyzed external rectus and the right eye fixes a light directly forward, the image of the right eve will remain stationary even though it is forcibly abducted or adducted. If the right eye is abducted, the red image before the left eye will move to the right; if adducted, to the left. In postural movements the close relationship between the external rectus and the vestibular mechanism is

emphasized. Three-dimensional spacial estimation of the individual to his surroundings is accomplished largely by coordinated movements of the eyes, head and body. Supranuclear integration of this complex process apparently occurs near the pontine centers of the external rectus and vestibular nuclei. Another interesting concept mentioned concerns the extraordinary sensitiveness to light of the extraocular muscles, especially the external rectus. Chas. A. Bahn.

Lyle, T. K. Latent nystagmus. Tr. Ophth. Soc. U. Kingdom 68:187-195, 1948.

Latent nystagmus occurs when one eye is covered or vision otherwise embarrassed. The cause is unknown. Usually it is associated with overt or latent strabismus. Six patients with the condition are reported. It is important to test the visual acuity with both eyes uncovered as well as in each eye separately. The inadvisability of carrying out occlusion to improve the visual acuity of the partially amblyopic eye is emphasized.

Beulah Cushman.

Neuschuler, I. A simplification of Duverger's advancement operation. Atti d. 37 Congresso Soc. oftal. ital. 10:197-199, 1948.

The author has found it advantageous to use a suture preplaced through the sclera near the original insertion. This suture is then placed through the belly of the muscle and incarcerates the tendon.

Frederick C. Blodi.

Pflugfelder, M., and Hauser, F. Complete paralysis of gaze in poliomyelitis. Ophthalmologica 118:378-382, Oct.-Nov., 1949

During a poliomyelitis epidemic a fiveyear-old boy came down with an acute febrile disease in the course of which he developed complete fixation of gaze with mask-like face and deficient lid closure which results in bilateral corneal ulcers (e lagophthalmo). Complete recovery ensued in about two months. A fairly diffuse poliomyelitic lesion of the central gray substance in the region of the rhombencephalon could account for the symptoms.

Peter C. Kronfeld.

Roelofs, C. O. The normal and the abnormal function of the superior oblique. Ophthalmologica 118:389-406, Oct.-Nov., 1949.

The author has described his approach to the subject of the normal function of the superior oblique in several previous publications. The approach is based, on the one hand, on a strict mathematical analysis of the muscle action within a three dimensional system of coordinates and, on the other hand, on the assumption that the human eve moves in accordance with the Listing's law. Roelofs has calculated the relative forces contributed or expended by each of the six extraocular muscles during movement in any of the eight cardinal directions. In the case of the superior oblique the greatest contribution is made on looking straight down. In all other directions the effort is less, decreasing in the following order: down and in, down and out, out and, finally, in. The view that the inferior oblique serves primarily for looking down and in, is undoubtedly incorrect, because that kind of movement would not conform with Listing's law.

The diagnosis of recent paralyses of the superior oblique is relatively easy. In cases of long standing hyperfunction or hypofunction of other eye muscles may complicate the picture. Nine illustrative cases are reported. Peter C. Kronfeld.

Scobee, R. G., and Bennet, E. A. Hyperphoria: a statistical study. Arch. Ophth. 43:458-465, March, 1950.

The authors examined 1,476 private pa-

tients with the Maddox rod test in an effort to obtain statistical information on hyperphoria and its clinical significance. They found that one in three patients may be expected to have hyperphoria of 0.5 diopters or more, while only one in twenty has a hyperphoria which is clinically significant. The prescribing of vertical prisms increased the manifest hyperphoria in only 18 percent of the patients, while 82 percent showed no change in the amount present after wearing vertical prisms constantly. Stevens described mild amblyopia in one eye as a symptom associated with hyperphoria, but this series revealed that 85 percent of the patients with hyperphoria had equal vision in each eye. No relation between lateral phoria and clinically significant hyperphoria was found. The etiology is not discussed in detail. The order of frequency of the involved muscles was: inferior oblique, superior oblique, superior rectus, and inferior rectus.

E. J. Swets.

Steckler, M. I. The problem of crosseye. Ann. Western Med. and Surg. 4: 196-197, April, 1950.

The author reviews many of the misconceptions of the laity regarding ocular muscle surgery and gives the proper information for parents. The psychologic background of the cross-eyed child may often be complex and is usually corrected with successful eye treatment. For the general physician it is important to know that a spontaneous cure very rarely occurs, that the condition responds well to treatment and that surgery is not always indicated. These patients should be referred as early as possible to the ophthalmologist.

Orwyn H. Ellis.

Studte. A severe complication in strabismus operation. Klin. Monatsbl. f. Augenh. 116:83-84, 1950.

The right eye of a 6-year-old girl was

operated on for convergent strabismus. At first a graduated tenotomy on the right internal rectus muscle was made and two months later the right external rectus muscle was advanced energentically The wound healed normally. Two weeks later a white fibrous mass was noted in the upper temporal scleral quadrant, a region not operated upon. The white mass was scraped off. Toward evening a large mass of vitreous protruded from a lentil-sized hole in the sclera. The vitreous was absised and the hole was covered with a conjunctival flap. Penicillin injections saved the eyeball. The energetic advancement obviously caused a circulatory disturbance that resulted in scleral necrosis. R. Grunfeld.

Travers, T. B. The practical importance of abnormal retinal correspondence. Tr. Am. Acad. Ophth. pp. 561-564, May-June, 1950:

The only satisfactory treatment of abnormal retinal correspondence is corrective operation. The positive diagnosis is preferably made with a major amblyoscope to determine the presence or abscence of simultaneous binocular vision. Abnormal retinal correspondence is probable in squints of 30 degrees which begin before the age of 3 years. The likelihood increases with the angle of squint and decreases with the age of onset. If the squint begins after the age of 4 years, abnormal retinal correspondence is infrequent in convergent squints of less than 20 degrees, and divergent squints of less than 10 degrees. It exists more frequently in squints which are constant in amount. Appropriate surgical treatment squints before the age of 4 years is usually followed by a restoration of simultaneous binocular vision. Treatment with alternating occlusion, prisms, and orthoptic training is not justified as a routine measure. Chas. A. Bahn.

Vaughton, G., and Stewart, M. Treatment of convergent squint associated with hypermetropia. Brit. J. Ophth. 34:212-220, April, 1950.

The authors are orthoptists who state that the treatment of convergent squint associated with hypermetropia often depends on proper refraction and the wearing of glasses. In a large series, 72 percent of convergent squints were found to be straightened by the wearing of proper and full correction alone. It was found that the excessive accommodation in a patient was removed and the incidence of suppression was greatly reduced. Full correction very greatly minimized the chance of the development of abnormal retinal correspondence. It is important to relax the excessive convergence effort as suppression is reduced and the muscle tone improved.

In the treatment of the accommodational element it was found equally important to train the adduction immediately after fusion developed. Since accommodation and convergence are associated, it was found that stimulating the adduction helped to maintain and improve a strong fusion. Orwyn H. Ellis.

7

CONJUNCTIVA. CORNEA, SCLERA

Anastasi, Giovanni. A case of the xerophthalmic syndrome. Ann. di ottal. e clin. ocul. 76:45-51, Feb., 1950.

A case of the xerophthalmic syndrome observed in a 59-year-old man with atrophic cirrhosis of the liver is reported. Night blindness, Bitôt's spots, and keratomalacia with a corneal ulcer marked the successive stages. The genesis and evolution of the syndrome were linked with insufficient production of vitamin A by the liver. Parenteral administration of vitamin A in large doses resulted in amelioration. The case is discussed in the

light of our present-day knowledge of vitaminology. (References)

Harry K. Messenger.

Azzolini, U. Crysosis of the cornea. Giorn. ital. oftal. 3:95-108, March-April, 1950.

From his experimental work the author concludes that light influences the deposit of gold salts in the cornea and that this occurs only when the metal reaches the elastic tissue. The gold particles are spread earlier and more extensively on Descemet's membrane if there is exposure to light. It is probable, that the gold is deposited as a metal in the elastic tissue of the cornea. The author discusses the pathogenetic problem of gold deposit in the cornea and stresses the importance of pathologic changes of the vessels of the limbus. Vito La Rocca.

Babel, J. Accumulations of fatty materials in the cornea. Arch. d'opht. 10:5-20, 1950.

Babel reviews the literature on fat deposition in the cornea and describes four important types: 1, true xanthomatosis of the cornea with deposition of cholesterol crystals and without inflammatory changes, 2. primary steatosis, with recurrent inflammatory signs, which the author considers a primary dystrophy in which the inflammation is a foreign body reaction to broken-down lipoidal material, 3. lipoidal accumulations secondary to an inflammatory process of long duration, such as trachoma, interstitial keratitis, or sclerokeratitis, and 4. fat depositions in tissue undergoing rapid necrosis, as in a poorly cicatrized corneal graft undergoing elimination. Case histories are used to illustrate the different types and photomicrographs of sections, four in color, illustrate their histopathology.

The author notes that the nature of the lipoidal material varies and that usually there is a mixture. Neutral fats, cholesterol, esters of cholesterol, fatty acids, cerebrosides, and phosphatids have been encountered. He concludes that X-ray treatment is helpful in corneal steatosis but that corneal grafts offer the only help in the other types.

Phillips Thygeson.

Barraquer Moner, J. I. A new technique of fixing the corneal graft in perforating keratoplasty. Atti d. 37 Congresso Soc. ital. oftal. 10:53-57, 1948.

The greater number of biological problems in keratoplasty are connected with the technique of the section and above all with the fixation of the corneal graft. The author uses the direct corneo-corneal sutures. As this method is connected with a considerable degree of trauma to the graft, a new technique has been tried on experimental animals.

The first step consists in cutting out with a 4 mm, trephine the anterior third of the cornea in the central area. Then a rectangular flap of the anterior third of the cornea is prepared measuring 9 mm. in width. This flap is dissected downward and remains adherent to the cornea at its lower border. This flap will be perforated in its center by the first trephine cut. Then a 6 mm. penetrating grafting is performed in the center of the cornea. After the donor tissue is in place the rectangular flap is turned upward again and the upper border of this flap sutured to the cornea. The transplant is therefore kept in position by the overlapping border of the first and smaller trephine.

Frederick C. Blodi.

Biocca, P., and Missiroli, G. X-ray pictures of the thymus gland in patients with vernal conjunctivitis. Atti d. 37 Congresso Soc. ital. oftal. 10:60-62, 1948.

Four of 10 patients showed persistence and hypertrophy of the thymus gland.

Frederick C. Blodi.

Bjorkenheim, Barbro. The pathogenesis of eye phlyctenules with special reference to the role of B-hemolytic streptococci. Acta ophth. 27:437-454, 1949.

The material for the study comprised 122 patients with phlyctenules, ranging from infancy to 62 years of age, and 40 patients with acute external diseases of the eye for control. Many members of the families show that the family histories of patients with phlyctenulosis had tuberculosis. All but 3 percent of the patients reacted positively to the Mantoux test and with greater intensity than the controls, and 56 percent had clinical evidence of healed tuberculosis. An increased antistreptolysin titer was found in 70 percent of the patients with phlyctenulosis, and in 13 percent of those without, B-hemolytic streptococci were cultured from pharyngeal swabs of 37 percent of patients with phlyctenulosis. None were found in the control material. The high incidence of increased antistreptolysin titer is interpreted as an indication that the streptococci were responsible for the onset of phlyctenulosis. Ray K. Daily.

Carapancea, Mihai. A new biologic approach in partial keratoplasty; respect for the bioarchitecture of the cornea. Arch. d'opht. 10:51-57, 1950.

Carapancea believes that opacification of the graft in partial, nonpenetrating keratoplasty results in many instances from failure to respect the optical and mechanical zones of the cornea. He divides the cornea into five zones which he illustrates by diagram. The most anterior zone, zone 1, has in the area of the pupil 6.11 percent of the thickness of the cornea, zone 2 has 2.17 percent, zone 3 has 90 percent, zone 4 has 0.95 percent, and zone 5 has 0.64 percent. These zones vary somewhat in the periphery. He stresses the necessity for maintaining the correct alternation of the zones in the transplan-

tation technique. Simple quantitative replacement of tissue does not suffice.

Phillips Thygeson.

Castroviejo, R. Keratoplasty in treatment of keratoconus. Arch. Ophth. 42: 776-800, Dec., 1949.

Partial penetrating keratoplasty is the treatment of choice in advanced keratoconus. The ectatic area of cornea should be entirely replaced by graft if possible. This frequently requires an unusually large graft. The difficulties are discussed and the surgical technique is described in detail. The large grafts increase the danger of anterior synechiae. Methods of avoiding this complication and means of coping with it are described. When a suitable technique is used, the percentage of cases in which vision is greatly improved permanently should be high, from 75 to 90 percent. (17 figures)

John C. Long.

Cogan, D. G. A new method for studying endothelial regeneration. Ophthalmologica 118:440-443, Oct.-Nov., 1949.

There is little doubt from either the pathologic or experimental point of view that those epithelial disturbances characterized by the ultimate development of bullous keratitis are due to absence or impaired function of the corneal endothelium. Few experiments have been made on regeneration of the endothelium because of its relative inaccessibility. Cogan's method of gaining access to the endothelium and inflicting a measurable amount of damage consists of inserting a tiny magnetic foreign body (angulated chips of paper clips, about 1 mm. long) into the anterior chamber by means of which, 2 to 3 weeks later, the endothelium is damaged or abraded over strip-shaped portions of the cornea by carrying a magnet across the anterior corneal surface. This endothelial injury is followed by the typical localized swelling and opacity of

the cornea which, within a week or two, subsides again, presumably because of regeneration of the endothelium.

Peter C. Kronfeld.

Dekking, H. M. The use of hyaluronidase in some corneal affections. Ophthalmologica 119:63-64, Jan., 1950.

Aqueous solutions of hyaluronidase (5 turbidity-reducing units per cc.) instilled into the conjunctival sac 4 or 5 times a day proved very effective in filamentary and punctate superficial keratitis.

Peter C. Kronfeld.

Eleftheriou, D.-S., and Djacos, C. Anatomo-pathologic lesions of the cornea in the edemas of starvation. Arch. d'opht. 10:217-227, 1950.

The authors supplement previous clinical studies on the corneal changes occurring in the edema of starvation by reporting on the histopathology of the cornea in autopsy material from five fatal cases. They note that the only part of the eve affected was the cornea, and to these corneal alterations they have given the name "superficial polymorphous keratopathy." These alterations are extremely polymorphous, varying from simple intraepithelial or subepithelial punctiform lesions to loss of large areas of epithelium. Histopathologic descriptions of the epithelial lesions are detailed and illustrated by photomicrographs. The lesions consisted of intercellular edema with compression of cells by the liquid, degenerative changes in the nuclei and cytoplasm, and such other changes as epithelial erosions due to necrosis of cells and areas of facet-forming epithelial thinning. No frank ulcerations were observed and there was no infiltration with inflammatory cells. Special lesions were observed in the periphery of the cornea, appearing as foci with diameters up to 2 mm. Microscopically these lesions consisted in replacement of the corneal lamellae by a

homogeneous substance taking a grayviolet color with hematoxylin. Over these areas the epithelium was sometimes absent but it was more often irregular and of varying thickness. The authors discuss the pathogenesis of the corneal lesions and conclude by referring to the parallel studies of Petzetakis and Spyratos.

Phillips Thygeson.

Faldi, Silvano. Coats' ring. Giorn. ital. oftal. 3:146-153, March-April, 1950.

The author reports a case of Coats' white corneal ring, localized as usual in Bowman's membrane. He suggests that this formation might result from incomplete resorption of the superficial layers of the vitreous and that it is comparable to the residual hyaloid artery on the posterior surface of the lens.

Vito La Rocca.

Ferrata, L., and Morpurgo, F. Original techniques in keratoplasty. Giorn. ital. oftal. 3:128-132, March-April, 1950.

The authors describe a satisfactory technique for keratoplasty in rabbits as well as the difficulties encountered, and the methods used to solve these problems.

Vito La Rocca.

Ferrata, L., and Morpurgo, F. Experimental research in keratoplasty. Giorn. ital. oftal. 3:188-203, May-June, 1950.

The authors present an experimental study on keratoplasty, with sections showing normal healings as well as operative complications. They believe that in successful cases the intercellular structures of the graft are accepted and persist. The epithelium and endothelium are partially replaced by migration of the cells of the recipient corneas. The stromal cells partially degenerate and newly formed keratoblasts are of doubtful origin. In cloudy grafts, the sections show a massive degeneration and replacement of the transplanted tissues. In other cases,

there is a growing of newly formed connective tissue in the graft or on its posterior surface, especially when there is anterior synechia. Vito La Rocca.

Francia, Corrado. Keratitis in Hodgkin's disease. Rassegna ital. d'ottal. 19: 140-150, March-April, 1950.

Francia found only four previous cases of corneal involvment in Hodgkin's disease in the literature. His patient was a 26-year-old man, who during his military duty developed malaria with anemia and chronic enterocolitis. Shortly after, he noticed swelling of the lymph nodes in the lateral cervical region. The swelling gradually increased and other swollen glands were found in the axilla and groin. There were periods of remission but four years later severe keratitis appeared, first in one eye and later in the other. Scrapings of the conjunctiva showed abnormal epithelial cells in tumultuous proliferation. with atypical mitoses. These cells appeared after radiation but may not have been due to this agent. Only histologic examination of the cornea would prove whether the changes were typical of Hodgkin's disease. There was a scarcity of cells in the reticulo-endothelial system of the cornea. With radiation and massive doses of vitamins B1 and B2, the patient recovered his health and useful vision.

Eugene M. Blake.

François, J., Kluyskens, J., and Rabaey, M. Intra-epithelial epithelioma of the conjunctiva and the cornea (Bowen's disease) healed by contact radiotherapy. Brit. J. Ophth. 34:360-364, June, 1950.

A patient with Bowen's disease was successfully treated by contact radio-therapy. No damage was done to the eye which has remained normal for six months following treatment. The literature is reviewed. The diagnosis had been confirmed by biopsy. (2 photomicrographs)

Orwyn H. Ellis.

Friede, Reinhard. The pathogenesis of the true pterygium. Acta ophth. 27:507-515, 1949.

The author presents a new theory according to which pterygium is the end result of a pathologic process which involves the conjunctiva, the episclera and the cornea. Chronic conjunctivitis is the predisposing factor; the perilimbal episcleritis the exciting factor, and the cornea assumes the task of producing the clinical picture of progressive pterygium. The conjunctival process is of years' duration, the episcleral irritation is an acute, transitory, relatively short episode, and the corneal phase is again of a slow chronic type when the episcleritis is no longer present. Chronic conjunctivitis leads to changes in the tissue and secretion of the conjunctival surface; the pressure of the lids on the eyeball, which is more pronounced in the nasal side, produces tissue edema on the nasal side of the interpalpebral zone, which is the precursor of hyaline changes; the density of the connective tissue in the region of the internal rectus, the stagnation of tears incident to this region, and the atmospheric changes to which the interpalpebral zone is exposed predispose to chronic inflammatory processes. These changes invade the adjacent episclera, from where they extend into the sublimbal region of the cornea. The postscleritic sublimbal infiltrates are then forced by a pressure mechanism of the lids towards the center of the cornea. To demonstrate that a bacterial factor plays no role in the development of the pterygium, the author used a surgical procedure, which could have no effect on bacterial activity. He left the head of the ptervgium attached to the cornea while retroplanting the body and neck. The head of the pterygium slowly became flatter, less defined and finally disappeared by absorption. Ray K. Daily.

Gallenga, Riccardo. Partial lamellar

keratoplasty. Rassegna ital. d'ottal. 19:3-7. Jan.-Feb., 1950.

Gallenga employs a .5-mm. or larger trephine with an internal piston which permits consistent penetration of host and donor cornea. The disc is raised from the edge by very fine forceps and dissected free with Landolt's knife. This permits the operator to see clearly the plane of dissection. The host's bed is prepared first and is ready for the lamellar graft from the donor, preferably a cadaver. Singleneedle sutures are used and two cross the implant. The suture begins over the ciliary body, reaches almost to the limbus on the opposite side, where a good bite of cornea is secured, and then turns back to the starting point. A vertical and horizontal suture are thus placed. The evelids are sutured together to obtain firm pressure. The writer employs lamellar grafting in all painful conditions of the cornea, including herpetic keratitis, kerato-hypopyon and Mooren's ulcer. No statistics are given as to percentages of "takes" or visual results.

Eugene M. Blake.

Gallenga, Riccardo. Corneal transplants in kerato-hypopyon. Rassegna ital. d'ottal. 19:73-76, March-April, 1950.

Eight cases of severe hypopyon ulcers were treated by lamellar transplantation. Cleavage was obtained down to Descemet's membrane. In three of the patients the cornea had been perforated but transplantation yielded one clear transparent disc, one partially opaque and one which was totally clouded. In all eight cases, the globes were preserved. 4 transplants were perfectly clear, 1 partially so, 2 opaque and moderately vascularized, 1 opaque with marginal iris adhesions. Relief of pain was prompt in all and all received injections of penicillin for seven days post-operatively. Eugene M. Blake.

Glees, M. The familial appearance of

primary band-shaped corneal degeneration, Klin. Monatsbl. f. Augenh. 116:185-187, 1950.

Almost identical forms of primary corneal degeneration were seen in father and son. The son's blood-calcium level was considerably increased. The father died suddenly and his blood-calcium level could not be determined. Thus the question of familial tendency and the role blood calcium plays remained undetermined.

R. Grunfeld.

Hartleib, Robert. Corneal suture or conjunctiva flap? Klin. Monatsbl. f. Augenh. 116:192-199, 1950.

The advantage of conjunctival flap lies in its ease of handling, but it covers the wound and prevents observation. A clear-cut corneal or scleral wound, if it is not longer than 6 mm, is best sutured directly. If the wound is longer than 6 mm, or irregular, of zigzag form, or if there is loss of corneal substance it must be covered by a conjunctiva flap.

R. Grunfeld.

Jackson, C. R. S. Riboflavin deficiency with ocular signs: report of a case. Brit. J. Ophth. 34:259-260, April, 1950.

A patient with a severe dietary deficiency responded very rapidly to riboflavin by mouth. A distinction must be drawn between the normal limbal capillary plexus and the appearances of new superficial vessels on the cornea. Failure to appreciate this distinction may be the cause of the large number of published cases. Although the disappearance of photophobia and regression of the abnormal vessels as a result of treatment may be striking, the improvement of visual acuity may be disappointing in long standing cases because of the persistence of corneal opacities.

Orwyn H. Ellis.

Kadin, Maurice. Metallic corneal

foreign bodies. Tr. Am. Acad. Ophth. pp. 392-393, March-April, 1950.

The author recommends removal of metallic corneal foreign bodies and accompanying rust rings under the slit-lamp. A 5-percent sulfonamide ointment is used routinely, and sometimes a mild mydriatic.

Gustav C. Bahn.

Kamel, Sabri. Primary tuberculosis of the conjunctiva. Brit. J. Ophth. 34:322-327, May, 1950.

Tuberculosis of the conjunctiva may originate exogenously as a primary infection or as a superimposed infection in a patient already infected elsewhere and endogenously from an established remote focus or by direct extension from a tuberculous lesion of a neighboring tissue. Tuberculous conjunctivitis may take any form but it is exceedingly rare and usually occurs in the first two decades of life. Diagnosis is best made by biopsy. A 10-year-old boy with primary ulcerous tuberculous conjunctivitis is described. Initial removal of the ucler by surgery probably caused an intraocular spread which resulted in a secondary retinal detachment. The patient was given 1 gram of streptomycin intramuscularly daily for 25 days and some ultraviolet radiation. Cure of the ulcer and of the detachment were essentially complete. Useful vision was restored. Morris Kaplan.

Kornerup, Tore. Epithelial cysts at the limbus in man. Acta ophth. 27:483-516, 1949.

Seven cases of epithelial cysts at the limbus, some situated in pterygia, are reported with histological data. (12 figures)

Ray K. Daily.

Kozlowski, Bogumil. A rare case of degeneration of the cornea. Klinika Oczna 18:521-530, 1948.

The author describes a case of bilateral peripheral circular corneal opacity in a young woman, 25 years of age. The opacity was vascularized. On the nasal side there was a fold of conjunctiva similar to a pterygium. Biopsy of corneal tissue revealed infiltration by fibrous tissue of the superficial layers of the cornea with destruction of Bowman's membrane. The infiltration was thicker near the limbus and contained plasma cells, lymphocytes and leukocytes. Complete examination of the patient did not give any clue as to the cause of the disease. There was only a slight imbalance of pituitary and sexual glands. The author considers that the process in the cornea was of a degenerative nature.

Sylvan Brandon.

Kraupa, E. Corneal infiltration due to tertiary syphilis. Ophthalmologica 119: 225-226, April, 1950.

The very rare keratitis due to tertiary syphilis may present the picture of deep pustuliform keratitis or the picture of a gummatous corneal infiltration which the author describes as follows. The lesion is a sharply outlined grayish-whitish disc, up to 1.5 mm. in diameter, situated in the superficial stroma. There is marked injection with severe pain at night but no visible iritis. The lesion and especially the pain responds promptly to iodides internally.

Peter C. Kronfeld.

Krukowska, Krystyna. The treatment of scrophulous keratoconjunctivitis with riboflavin. Klinika Oczna 18:549-550, 1948.

Two cases of severe scrophulous keratoconjunctivitis are described. Improvement followed 3 to 5 mgms, of riboflavin a day. Riboflavin acts by improving cellular respiration. Sylvan Brandon.

Larsen, V., and Eriksen, A. Cornea plana. Acta ophth. 27:275-286, 1949.

The histories of 13 cases in 3 generations of 2 unrelated families are reported, and the scanty literature on the subject

comprising 14 case reports is critically reviewed. These subjects had flat corneas, which merged into the sclera, with no clear line of demarcation at the limbus. or a gray limbal zone showing vascularization, a flattened anterior chamber, and a slight hypoplasia of the iris. The refraction was emmetropic in 4 cases, hyperopic in 6, and slightly myopic in 1. Three subjects had strabismus, 1 anisometropia, 1 cataract and 1 choroidal changes. It is shown that cornea plana is an isolated anomaly, not necessarily accompanied by microcornea or an anomaly of the retina and optic nerve and that it is genetically dominant, and not, as previously believed, recessive.

Ray K. Daily.

Miklós, A. Healing serpiginous ulcer of the cornea by total conjunctival hooding. Brit. J. Ophth. 34:335-350, June, 1950.

The author presents case reports of successful, prompt healing in severe serpiginous ulcers after hooding, which consists of a conjunctival flap drawn down from above, completely covering the cornea, and anchored at three places below the cornea. Grave ulcers did not respond to penicillin therapy, probably because of blockage of lymph circulation. The hood is not removed until the eye is absolutely pale and quiet which generally takes two to three months. The patient returns to work with the flap in place.

Orwyn H. Ellis.

Nataf, Roger. The etiology of trachoma. Ophthalmologica 118:687-700, Oct.-Nov., 1949.

The author is well known for his previous work in the field of trachoma. In the paper under review he sums up his work and that of other investigators which tends to point to the fact that the trachoma virus is a cell parasite which seems to belong to the class of Rickettsiae but differs in some respects from typical

Rickettsiae. The name Provazekia trachomatis is preferable to the older term Rickettsoid bodies. Peter C. Kronfeld.

Offret, G., and Chauvet, P. The study and treatment of vascularization of the cornea. Arch. d'opht. 10:344-366, 1950.

In an extensive study the authors have considered the problem of corneal vascularization under the following headings: 1. anatomy and clinical appearance, 2. pathology, 3. pathogenesis, and 4. therapy. The anatomy of the limbus region is considered in detail, and Busacca's classification of the limbus into the zone of terminal capillary loops and the palisade zone is accepted. The various types of corneal vascularization are considered and illustrated and it is interesting that interstitial vascularization is described as being much more complex than the superficial type, five different morphological forms being recognized. The pathology of corneal vascularization is described with particular reference to the cytology of different types of corneal inflammation. The problem is considered especially as related to the vascularization of corneal grafts after keratoplasty.

The second part of the study, in which pathogenesis and therapy are considered, is to be reported in the next issue.

Phillips Thygeson.

Sauvant, J. Peculiar parenchymatous corneal opacities of inconstant localization (keratitis periodica fugax). Klin. Monatsbl. f. Augenh. 116:199-206, 1950.

A 17-year-old boy had peculiar, inconstant interstitial corneal opacities of various, uncharacteristic forms, accompanied by similar inconstant areas of infiltrations in the episclera. The episcleritis seemed to be primary and the cornea was secondarily affected either by nutritional damage of by direct continuation of the episcleritis.

R. Grunfeld.

### **NEWS ITEMS**

Edited by DONALD J. LYLE, M.D. 601 Union Trust Building, Cincinnati 2

News items should reach the editor by the 12th of the month but, to receive adequate publicity, notices of postgraduate courses, meetings, and so forth should be received by the editor at least three months before the date of occurrence.

#### DEATHS

Dr. Albert Arthur Carter, Boston, Massachusetts, died June 23, 1950, aged 76 years.

Word has been received from Dr. Georg W. Keyser of Oslo, Norway, that Harald Lystad, a distinguished pupil of Professor Schiptz, passed away on May 21, 1950, at the age of 75 years, in Oslo, where he had practiced during his entire career. Lystad's wide interests included a great love of travel and music. He served as a member of the council of the Philharmonic Society from 1933 to 1941 and was a musical reporter for the local papers. Lystad has the distinction of being the only ophthalmologist yet appointed to the presidency of the Norwegian Union of Physicians.

### ANNOUNCEMENTS

#### GILL HOSPITAL COURSE

The Gill Memorial Eye, Ear, and Throat Hospital, Roanoke, Virginia, announces the twenty-fourth annual spring congress to be held at the hospital from April 2 to 7, 1951. Among the guest speakers will be:

Dr. Edwin N. Broyles, Baltimore; Dr. E. C. Kendall, Rochester, Minnesota; Dr. Paul Holinger, Chicago; Dr. John R. Lindsay, Chicago; Dr. Lawrence Pool, New York; Dr. D. H. Anthony, Memphis; Dr. Robert H. Sinskey, Durham, North Carolina; Dr. J. A. Sullivan, Ontario, Canada; Dr. Robert H. Trueman, Philadelphia; Dr. William P. McGuire, Winchester, Virginia; Dr. Harold Scheie, Philadelphia; Dr. R. W. Hollenhorst, Rochester, Minnesota; Dr. Wendell Hughes, Hempstead, New York; Dr. J. Gordon Cole, New York; Dr. Harvey Thorpe, Pittsburgh; Dr. Bryon Smith, New York; Dr. A. D. Ruedemann, Detroit; and Dr. Edwin Burton, Charlottesville, Virginia.

### ASSUMPTION OF COMMMAND

The President of the United States of America announces the appointment of Col. Elbert DeCoursey (MC) as Director of the Armed Forces Institute of Pathology, Washington, D.C., effective August 1, 1950.

### MISCELLANBOUS

### CALIFORNIA COURSE

Officers of instruction for the ophthalmology course recently given at the University of California School of Medicine were:

Dr. Samuel D. Aiken, Dr. Crowell Beard, Dr. Dudley P. Bell, Dr. George S. Campion, Dr. Joseph W. Crawford, Dr. C. Allen Dickey, Dr. Owen C. Dickson, Miss Elva Mary Florrid, Dr. Levon K. Garron, Dr. David O. Harrington, Dr. Margaret Henry, Dr. Michael J. Hogan, Dr. Robert N. Shaffer, Dr. Joseph G. Smith, Dr. Phillips Thygeson, and Dr. Edwin Wortham.

### SOCIETIES

#### ELECT OFFICERS

The Medical Association of the Institute Penido Burnier, Campinas, Brazil, announces the election of the following officers for the year, 1950-1951:

President, Dr. Alfonso Ferreira Filho; first secretary, Dr. Francisco A. Mais; second secretary, Dr. R. Burgos Pimentel; treasurer, Dr. L. de Souza Queiroz; commissioners: Dr. Penido Burnier, Dr. Gabriel Pôrto, and Dr. Penido Burnier Filho.

#### PERSONALS

On July 12, 1950, the Royal College of Surgeons of Edinburgh presented honorary fellowships to Dr. H. Arruga of Barcelona, to Sir Stewart Duke-Elder of London, and to Dr. Alan C. Woods of Baltimore.

The following week, the Royal College of Surgeons of England conferred honorary fellowships on Dr. Jean-Pierre Bailliart of Paris, and Dr. Derrick Vail of Chicago.

Dr. Alston Callahan presented two lectures on surgical repair of eyelid injuries to the Finnish Ophthalmological Society, Helsinki, Finland, in July.

Dr. James W. Smith, New York, has been elected New York regional director of the National Society of Autograph Collectors. Many medical and ophthalmologic references appear in Dr. Smith's collection of original letters written by presidents of the United States. The Guild of Prescription Opticians of America, Inc.

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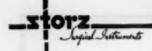
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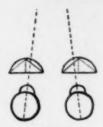
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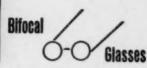
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# ConAcor IS A TECHNICAL IMPROVEMENT!







Prism base out at converging point in plus lens neutralized with ConAcor Bifocal Segment,

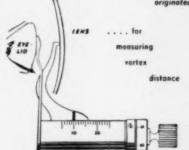
ConAcor has America talking about optical center control: Its precision design assures trial lens comfort at near point. The ConAcor lens is a special bifocal originated and developed by Austin Belgard for "individualized" optical center control.

When optical center control is needed for a true translation of your prescription, ConAcor is the accepted lens.

Wholesale Rx service to eye physicians and dispensing opticians.

### The Belgard Lenscorometer

originated by Austin Belgard



Use of Lenscorometer in all cases of Aphakia, + OR - corrections of four diopters or more—a necessity to insure true translation of prescription.

Each \$11.75



109 N. Wabash, at Washington

(Formerly Belgard, Inc.)

9th Floor

STate 2-5362

The NEW

MONOPLEX

integrated

IMPLANT

The small, round cut-back neck permits purse-string suturing. Plastic lip protects area of conjunctiva where it is drawn around the neck. The placement of the tantalum mesh over a series of channeled grooves in the plastic simplifies suturing of the muscles and permits a firm attachment of tissue. The large area of smooth acrylic plastic on the posterior portion facilitates motility.



Simple symmetrical design

proven advantages

Write American Optical Company, Dept. CP-AM, Southbridge, Mass., for "Technique of Enucleation", Monoplex Implant, written by Dr. Jay G. Linn, Jr.

American Optical